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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  MAY 01  New CAS web site launched
 NEWS  3  MAY 08  CA/CAplus Indian patent publication number format defined
 NEWS  4  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                  fields
 NEWS  5  MAY 21  BIOSIS reloaded and enhanced with archival data
 NEWS  6  MAY 21  TOXCENTER enhanced with BIOSIS reload
 NEWS  7  MAY 21  CA/CAplus enhanced with additional kind codes for German
                  patents
 NEWS  8  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                  patents
 NEWS  9  JUN 27  CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 10  JUN 29  STN Viewer now available
 NEWS 11  JUN 29  STN Express, Version 8.2, now available
 NEWS 12  JUL 02  LEMBASE coverage updated
 NEWS 13  JUL 02  LMEDLINE coverage updated
 NEWS 14  JUL 02  SCISEARCH enhanced with complete author names
 NEWS 15  JUL 02  CHEMCATS accession numbers revised
 NEWS 16  JUL 02  CA/CAplus enhanced with utility model patents from China
 NEWS 17  JUL 16  CAplus enhanced with French and German abstracts
 NEWS 18  JUL 18  CA/CAplus patent coverage enhanced
 NEWS 19  JUL 26  USPATFULL/USPAT2 enhanced with IPC reclassification
 NEWS 20  JUL 30  USGENE now available on STN
 NEWS 21  AUG 06  CAS REGISTRY enhanced with new experimental property tags
 NEWS 22  AUG 06  BEILSTEIN updated with new compounds
 NEWS 23  AUG 06  FSTA enhanced with new thesaurus edition
 NEWS 24  AUG 13  CA/CAplus enhanced with additional kind codes for granted
                  patents
 NEWS 25  AUG 20  CA/CAplus enhanced with CAS indexing in pre-1907 records

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

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FILE 'HOME' ENTERED AT 13:27:10 ON 21 AUG 2007

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:27:52 ON 21 AUG 2007
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STRUCTURE FILE UPDATES:   20 AUG 2007  HIGHEST RN 945102-95-4
DICTIONARY FILE UPDATES:  20 AUG 2007  HIGHEST RN 945102-95-4

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

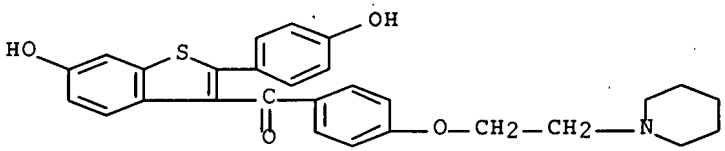
=> e raloxifene/cn
E1            1     RALOX LC/CN
E2            1     RALOX-A/CN
E3            1 --> RALOXIFENE/CN
E4            1     RALOXIFENE HYDROCHLORIDE/CN
E5            1     RALOZAM/CN
E6            3     RALSTONITE/CN
E7            1     RALSTONITE (ALF2(OH))/CN
E8            1     RALSTONITE (ALF2(OH).1/2H2O)/CN
E9            1     RALTAT 10/CN
E10           1     RALTEGRAVIR POTASSIUM/CN
E11           1     RALTITREXED/CN
E12           1     RALUBEN/CN

=> s e3
L1            1 RALOXIFENE/CN

=> d l1 1 ide

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   84449-90-1  REGISTRY
ED   Entered STN:  16 Nov 1984
```

CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]- (CA INDEX NAME)
OTHER NAMES:
CN Keoxifene
CN LY 139481
CN **Raloxifene**
CN [2-(4-Hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-(2-(1-piperidinyl)ethoxy)phenyl]methanone
MF C28 H27 N O4 S
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1751 REFERENCES IN FILE CA (1907 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1763 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.25	8.46

FILE 'CAPLUS' ENTERED AT 13:29:27 ON 21 AUG 2007

FILE COVERS 1907 - 21 Aug 2007 VOL 147 ISS 9
FILE LAST UPDATED: 20 Aug 2007 (20070820/ED)

They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l1
L2 1763 L1

=> d scan

L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 1-0 (Pharmacology)
TI Osteoporosis treatment and limitations and perspectives
ST review bisphosphonate raloxifene parathyroid hormone fall prevention disuse syndrome
IT Bone, disease
(fracture; osteoporosis treatment and limitations and perspectives)
IT Anabolic agents
Osteoporosis
(osteoporosis treatment and limitations and perspectives)
IT Diphosphonates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoporosis treatment and limitations and perspectives)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bisphosphonate; osteoporosis treatment and limitations and perspectives)
IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(osteoporosis treatment and limitations and perspectives)
IT **84449-90-1**, Raloxifene 129318-43-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoporosis treatment and limitations and perspectives)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 1-1 (Pharmacology)
TI Validation of a novel HPLC method for the determination of Raloxifene and its pharmacokinetics in rat plasma
ST Raloxifene detn plasma HPLC; liq chromatog Raloxifene plasma; pharmacokinetics Raloxifene plasma
IT Blood plasma
Pharmacokinetics
(pharmacokinetics of Raloxifene in blood plasma of rats after oral dose)
IT Blood analysis
HPLC
(validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma)
IT **84449-90-1**, Raloxifene
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN

CC 1-8 (Pharmacology)
TI Effect of genistein and raloxifene on vascular dependent platelet aggregation
ST genistein raloxifene antiplatelet platelet aggregation blood vessel
IT Blood vessel
Cardiovascular system, disease
Platelet aggregation
Platelet aggregation inhibitors
(effect of genistein and raloxifene on vascular dependent platelet aggregation)
IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)
IT Phytoestrogens
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)
IT 9001-84-7, Phospholipase A2 10102-43-9, Nitric oxide, biological studies 35121-78-9, Prostacyclin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)
IT 446-72-0, Genistein **84449-90-1**, Raloxifene
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1/prep
1763 L1
4449106 PREP/RL
L3 38 L1/PREP
(L1 (L) PREP/RL)

=> d l3 4 ibib abs

L3 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1180831 CAPLUS Full-text
DOCUMENT NUMBER: 145:356564
TITLE: The advance of synthetic studies on selective estrogen receptor modulators
AUTHOR(S): Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan
CORPORATE SOURCE: Fourth Brigade of Pharmacy, Medical College of Chinese People's Armed Police Force, Tianjin, 300162, Peop. Rep. China
SOURCE: Wujing Yixueyuan Xuebao (2005), 14(2), 151-156
CODEN: WYXUA9; ISSN: 1008-5041
PUBLISHER: Wujing Yixueyuan Xuebao Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl)stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

=> d l3 ibib abs 1-
YOU HAVE REQUESTED DATA FROM 38 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:70746 CAPLUS Full-text
DOCUMENT NUMBER: 147:172240
TITLE: Control of pharmaceuticals and animal health products in wastewater effluents from manufacturing sites
AUTHOR(S): Parke, Neil J.; Good, Nanci F.; Meyerhoff, Roger D.
CORPORATE SOURCE: Lilly Corporate Center, Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: WEFTEC.05, Conference Proceedings, Annual Technical Exhibition & Conference, 78th, Washington, DC, United States, Oct. 29-Nov. 2, 2005 (2005), 145-155. Water Environment Federation: Alexandria, Va.
CODEN: 69JOAM
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English
AB In many cases, the discharge of pharmaceuticals and animal health products at bulk manufacturing, fill/finish, development and research operations may not be directly regulated with numeric limitations as a part of a facility's wastewater discharge permit. The biol. activity of these discharged compds., if not properly managed, may have the potential to impact the operation of an onsite or a municipal wastewater treatment plant, aquatic species in streams, rivers, oceans, or a drinking water source. An overview of the Eli Lilly and Company environmental protection program is provided, which shows how potential releases of active ingredients from its operations are managed to protect the environment.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1063108 CAPLUS Full-text
DOCUMENT NUMBER: 145:417029
TITLE: Methods for generating stably linked complexes composed of homodimers, homotetramers or dimers of dimers
INVENTOR(S): Chien, Hsing Chang; Goldenberg, David M.; McBride, William J.; Rossi, Edmund A.
PATENT ASSIGNEE(S): IBC Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006107617	A2	20061012	WO 2006-US10762	20060324

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US 2007086942 A1 20070419 US 2006-478021 20060629
WO 2007046893 A2 20070426 WO 2006-US25499 20060629
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US 2007087001 A1 20070419 US 2006-581287 20061016
WO 2007047609 A2 20070426 WO 2006-US40431 20061016
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KG, KZ, MD, RU, TJ, TM

US 2007140966 A1 20070621 US 2006-633729 20061205
WO 2007075270 A2 20070705 WO 2006-US46367 20061205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2005-668603P	P	20050406
US 2005-728292P	P	20051019
US 2005-751196P	P	20051216
US 2006-782332P	P	20060314
US 2005-389358	A2	20060324
US 2006-389358	A	20060324
WO 2006-US10762	A	20060324
US 2006-391584	A2	20060328
WO 2006-US12084	A	20060329
US 2005-478021	A2	20060629
US 2006-478021	A	20060629
WO 2006-US25499	A2	20060629
US 2006-864530P	P	20061106

AB The authors disclose dimerization and docking domain (DDD) sequences for the generation of stably tethered structures of defined compns., which may have multiple functionalities and/or binding specificities. The tethered constructs may be virtually any mol. or structure, such as antibodies, antibody fragments, antibody analogs or mimetics, aptamers, binding peptides, fragments of binding proteins, known ligands for proteins or other mols., enzymes, detectable labels or tags, therapeutic agents, toxins, pharmaceuticals, cytokines, interleukins, interferons, radioisotopes, proteins, peptides, peptide mimetics, polynucleotides, RNAi, oligosaccharides, natural or synthetic polymeric substances, nanoparticles, quantum dots, organic or inorg. compds., etc. In one example, a fusion construct of a DDD sequence with an anti-CEA Fd fragment was prepared and shown to target colorectal cancer in a xenograft model.

L3 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:958171 CAPLUS Full-text
DOCUMENT NUMBER: 147:9760
TITLE: Synthesis of raloxifene hydrochloride
AUTHOR(S): Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong, Ping
CORPORATE SOURCE: Shenyang Institute of Chemical Technology, Faculty of Pharmaceutical-Engineering, Shenyang, 110142, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2005), 14(7), 882-884
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3-methoxybenzenethiol and 4-methoxy-α-bromo acetophenone via five steps, including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

L3 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1180831 CAPLUS Full-text
DOCUMENT NUMBER: 145:356564
TITLE: The advance of synthetic studies on selective estrogen receptor modulators
AUTHOR(S): Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan
CORPORATE SOURCE: Fourth Brigade of Pharmacy, Medical College of Chinese People's Armed Police Force, Tianjin, 300162, Peop. Rep. China
SOURCE: Wujing Yixueyuan Xuebao (2005), 14(2), 151-156
CODEN: WYXUA9; ISSN: 1008-5041
PUBLISHER: Wujing Yixueyuan Xuebao Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl)stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

L3 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:708484 CAPLUS Full-text
DOCUMENT NUMBER: 143:221841
TITLE: Estrogen receptor ligands. Dihydrobenzoxathiin SERAMs with an optimized antagonist side chain
AUTHOR(S): Blizzard, Timothy A.; DiNinno, Frank; Chen, Helen Y.; Kim, Seongkon; Wu, Jane Y.; Chan, Wanda; Birzin, Elizabeth T.; Yang, Yi Tien; Pai, Lee-Yuh; Hayes, Edward C.; DaSilva, Carolyn A.; Rohrer, Susan P.; Schaeffer, James M.; Hammond, Milton L.
CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(17), 3912-3916
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:221841

AB An optimized side chain for dihydrobenzoxathiin SERAMs was discovered and attached to four dihydrobenzoxathiin platforms. The novel SERAMs show exceptional estrogen antagonist activity in uterine tissue and an MCF-7 breast cancer cell assay.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:451379 CAPLUS Full-text
DOCUMENT NUMBER: 142:487547
TITLE: Antiresorptive mutual salt of raloxifene and bisphosphonic acid
INVENTOR(S): Ha, Tae Hee; Kim, Won Jeoung; Yun, Sangmin; Kim, Cheol Kyung; Kim, Han Kyong; Suh, Kwee-Hyun; Lee, Gwan Sun
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005047282	A1	20050526	WO 2004-KR2954	20041115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2005046883	A	20050519	KR 2003-80494	20031114
EP 1689744	A1	20060816	EP 2004-800095	20041115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 2007082871	A1	20070412	US 2006-579199	20060512
PRIORITY APPLN. INFO.:			KR 2003-80494 A	20031114
			WO 2004-KR2954 W	20041115

OTHER SOURCE(S): MARPAT 142:487547

AB The mutual salt of raloxifene and bisphosphonic acid exhibits unexpectedly synergistic effects of two components to enhance bone mineral d. (BMD), control blood-calcium d., and lower the serum cholesterol level. For example, 3.2 g of alendronic acid was mixed with 5.0 g of raloxifene in 75 mL of ethanol/75 mL of water to obtain 6.5 g of raloxifene alendronate pentahydrate. A soft or hard capsule was prepared containing raloxifene alendronate pentahydrate 30 mg, lactose 215 mg, magnesium stearate 2 mg, and colloidal silica 3 mg. When given to female rats, the mutual salt of raloxifene and alendronic acid markedly enhanced BMD, bone stiffness, trabecular volume and bone volume, and also effectively controlled the blood cholesterol and calcium level through the synergic effects of its two components, as compared with the individual raloxifene hydrochloride or alendronate.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:617920 CAPLUS Full-text

DOCUMENT NUMBER: 142:463529

TITLE: Synthesis of raloxifene hydrochloride

AUTHOR(S): Gong, Ping; Zhao, Yanfang; Wang, Dun

CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China

SOURCE: Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113
CODEN: SYDXFF; ISSN: 1006-2858

PUBLISHER: Shenyang Yaoke Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

OTHER SOURCE(S): CASREACT 142:463529

AB Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4-hydroxyphenyl)benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3, saponification with 5M NaOH solution in methanol, and saltification with HCl. The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR, 13C NMR.

L3 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:292022 CAPLUS Full-text

DOCUMENT NUMBER: 140:309411

TITLE: Pharmaceutical compositions comprising raloxifene acid addition salts and/or solvates

INVENTOR(S): Karup, Gunnar Leo; Pedersen, Soren Bols

PATENT ASSIGNEE(S): A/S Gea Farmaceutisk Fabrik, Den.

SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004029046	A2	20040408	WO 2003-DK645	20030930
WO 2004029046	A3	20041014		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2499819	A1	20040408	CA 2003-2499819	20030930
AU 2003266940	A1	20040419	AU 2003-266940	20030930
AU 2003266940	B2	20070208		
EP 1546138	A2	20050629	EP 2003-747847	20030930
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NO 2005002100	A	20050629	NO 2005-2100	20050429
US 2006154966	A1	20060713	US 2005-528691	20050921
PRIORITY APPLN. INFO.:			DK 2002-1450 A	20020930
			WO 2003-DK645 W	20030930

OTHER SOURCE(S): MARPAT 140:309411

AB Raloxifene acid addn. salts or solvates thereof, having improved dissoln. properties in media comprising hydrochloric acid are described, compared with similar prepns. based on raloxifene or raloxifene-hydrochloride. The disclosed acid addition salts or solvates thereof show an improved bioavailability in media comprising hydrochloric acid, such as the gastric juice. The acid addition salts or solvates thereof are addition salts or solvates of raloxifene and a pharmaceutically acceptable acid selected among succinic acid, lactic acid, malonic acid or sulfuric acid. Further, crystalline forms of the raloxifene salts and solvates thereof are disclosed. The raloxifene acid addition salts and/or solvates thereof are useful for the preparation of pharmaceutical composition for oral administration capable of fast and reliable release of the active ingredients in the stomach of the patient, in particular for the treatment of cancer or osteoporosis, or for inhibiting cartilage degradation A new method for preparation of raloxifene lactate is also disclosed. Thus, raloxifene malonate was prepared by the reaction of raloxifene-HCl with malonic acid in propanol-water solution The product was characterized by IR spectra and x-ray diffraction.

L3 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:269853 CAPLUS Full-text
DOCUMENT NUMBER: 140:309370
TITLE: Amino acid and peptide carriers for oral delivery of active agent
INVENTOR(S): Piccariello, Thomas; Kirk, Randal J.; Olon, Lawrence P.
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 176 pp., Cont.-in-part of U.S. Pat. Appl. 2002 128,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004063628	A1	20040401	US 2002-156527	20020529
US 7060708	B2	20060613		
WO 2000052078	A1	20000908	WO 2000-US5693	20000306

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

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US 6716452 B1 20040406 US 2000-642820 20000822

US 2002099013 A1 20020725 US 2001-933708 20010822

US 2002128177 A1 20020912 US 2001-986426 20011108

US 7018654 B2 20060328

WO 2003034980 A2 20030501 WO 2001-US43089 20011114

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WO 2002051432 A1 20020704 WO 2001-US43115 20011116

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WO 2003020200 A2 20030313 WO 2001-US43117 20011116

WO 2003020200 A3 20030912

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WO 2003072047 A2 20030904 WO 2003-US5526 20030224

WO 2003072047 A3 20040617

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AU 2003216382 A1 20030909 AU 2003-216382 20030224

CA 2477088 A1 20031002 CA 2003-2477088 20030224

WO 2003079972 A2 20031002 WO 2003-US5524 20030224

WO 2003079972	A3	20040318			
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CN 1649614	A	20050803	CN 2003-808717		20030224
JP 2005524677	T	20050818	JP 2003-577805		20030224
IN 2003KN00329	A	20041009	IN 2003-KN329		20030320
WO 2003101476	A1	20031211	WO 2003-US17009		20030529
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IN 2004KN01318	A	20060616	IN 2004-KN1318		20040908
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US 2007060500	A1	20070315	US 2006-392878		20060330
PRIORITY APPLN. INFO.:			US 1999-265415	B2	19990310
			US 1999-411238	B2	19991004
			WO 2000-US5693	A	20000306
			US 2000-642820	A2	20000822
			US 2000-248620P	P	20001116
			US 2000-248659P	P	20001116
			US 2000-248660P	P	20001116
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US 2001-987458	B2	20011114
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US 2001-959396	B2	20011024
US 2002-358368P	P	20020222
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US 2004-953116	A2	20040930
US 2004-953119	A2	20040930
US 2004-955006	A2	20040930
WO 2004-US32131	A2	20040930

AB The present invention relates to oral delivery systems of active agent, and more specifically to compns. that comprise amino acids, as single amino acids or peptides, covalently attached to active agents and methods for oral administration of conjugated active agent compns. For example, a polyserine-furosemide conjugate was prepared and its in vivo performance was examined Compared to parent furosemide, the conjugate showed a sustained drug release. The 9 h serum level of the polyserine-furosemide conjugate was 95.5% of its 3

h level, whereas the 9 h serum level of the parent drug was only 59.8% of its 3 h level.

L3 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:726588 CAPLUS Full-text
DOCUMENT NUMBER: 139:345292
TITLE: Nitrosation, nitration, and autoxidation of the selective estrogen receptor modulator raloxifene by nitric oxide, peroxynitrite, and reactive nitrogen/oxygen species
AUTHOR(S): Toader, Violeta; Xu, Xudong; Nicolescu, Adrian; Yu, Linning; Bolton, Judy L.; Thatcher, Gregory R. J.
CORPORATE SOURCE: Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, 60612-7231, USA
SOURCE: Chemical Research in Toxicology (2003), 16(10), 1264-1276
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The regulation of estrogenic and antiestrogenic effects by selective estrogen receptor modulators (SERMs) provides the basis for use in long-term therapy in cancer chemoprevention and postmenopausal osteoporosis. However, the evidence for carcinogenic properties within this class requires study of potential pathways of toxicity. There is strong evidence for the elevation of cellular levels of NO in tissue treated with SERMs, including the benzothiophene derivative, raloxifene, in part via up-regulation of nitric oxide synthases. Therefore, the reactions of 17β-estradiol (E2), raloxifene, and an isomer with NO, peroxynitrite, and reactive nitrogen/oxygen species (RNOS) generated from NO2-/H2O2 systems were examined Peroxynitrite from bolus injection or slow release from higher concns. of 3-morpholinosydnonimine (SIN-1) reacted with the benzothiophenes and E2 to give aromatic ring nitration, whereas peroxynitrite, produced from the slow decomposition of lower concns. of SIN-1, was relatively unreactive toward E2 and yielded oxidation and nitrosation products with raloxifene and its isomer. The oxidation and nitrosation products formed were characterized as a dimer and quinone oxime derivative Interestingly, the reaction of the benzothiophenes with NO in aerobic solution efficiently generated the same oxidation products. Stable quinone oximes are not unprecedented but have not been previously reported as products of RNOS-mediated metabolism The reaction of glutathione (GSH) with the quinone oxime gave both GSH adducts from Michael addition and reduction to the corresponding o-aminophenol. The ready autoxidn. of raloxifene, observed in the presence of NO, is the first such observation on the reactivity of SERMs and is potentially a general phenomenon of significance to SERM chemical toxicol.
REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:491620 CAPLUS Full-text
DOCUMENT NUMBER: 139:179942
TITLE: Synthesis of Constrained Raloxifene Analogues by Complementary Use of Friedel-Crafts and Directed Remote Metalation Reactions
AUTHOR(S): Kalinin, Alexey V.; Reed, Mark A.; Norman, Bryan H.; Snieckus, Victor
CORPORATE SOURCE: Department of Chemistry, Queen's University, Kingston, ON, K7L 3N6, Can.
SOURCE: Journal of Organic Chemistry (2003), 68(15), 5992-5999

CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:179942
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB New constrained heterocyclic analogs of Raloxifene, I [R1 = 2-(1-piperidinyl)ethoxy, R2 = H; R1 = H, R2 = 2-(1-piperidinyl)ethoxy] and II, were prepared by complementary Directed remote Metalation (DreM)/Friedel-Crafts cyclization approaches. Utilization of a benzylidene-thiolactone rearrangement was successfully implemented to construct benzothiophenes III (R3 = Me2CH, R4 = MeO; R3 = Me, PhCH2, R4 = Et2N) in good yields. Selective deprotection of III (R3 = Me2CH, R4 = MeO; R3 = PhCH2, R4 = Et2N) induced by complexation was followed by trifluoromethylsulfonylation and Suzuki-Miyaura cross coupling with 3-[2-(1-piperidinyl)ethoxy]phenyl dioxaborolane to give the corresponding 2,4-diaryl-substituted benzothiophenes with methoxycarbonyl or diethylcarbamoyl group in the 3 position. Treatment of the latter with BCl3 or with excess LDA induced an intramol. para or ortho cyclization and concomitant double deprotection to furnish I. Similar sequence starting from III (R3 = Me, R4 = Et2N) afforded the constrained analog II.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:408662 CAPLUS Full-text
DOCUMENT NUMBER: 136:401637
TITLE: Preparation of 3-arylbenzothiophenes by cyclodehydration of phenylthioacetophenones using activated clay or zeolite catalysts.
INVENTOR(S): Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042289	A2	20020530	WO 2001-US42940	20011114
WO 2002042289	A3	20020906		
WO 2002042289	A8	20040212		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002030409	A5	20020603	AU 2002-30409	20011114

US 2004132775	A1	20040708	US 2003-415569		20030922
US 6921827	B2	20050726			
PRIORITY APPLN. INFO.:			US 2000-253212P	P	20001127
			WO 2001-US42940	W	20011114

OTHER SOURCE(S): CASREACT 136:401637; MARPAT 136:401637

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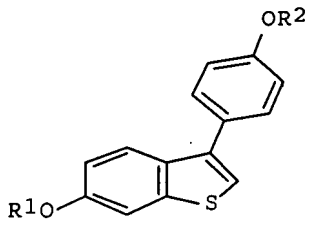
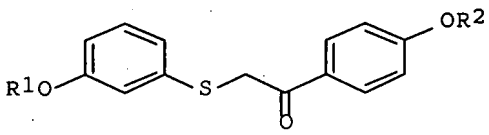


I



II

AB Title compds. (I; R1, R2 = H, protecting group) were prepd. by cyclodehydration of phenylthioacetophenones (II; variables as above) in the presence of acid activated clays or acid activated zeolites and in the presence of solvents. Thus, PhMe, α-(3-methoxyphenylthio)-4-methoxyacetophenone, and "acid-activated clay" (Engelhard X-9107) were combined and refluxed 2 h using a Dean Stark trap. By HPLC the product mixture consisted of 96.7% 6-methoxy-3-(4-methoxyphenyl)benzo[b]thiophene, 1.1% 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene, 2.1% 4-methoxy-3-(4-methoxyphenyl)benzo[b]thiophene, and 0.1% 4-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene.

L3 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:408636 CAPLUS Full-text

DOCUMENT NUMBER: 136:401533

TITLE: Coupling reaction process for preparing α-(3-arylthio)acetophenones from thiophenol derivs. and α-(leaving group)-substituted acetophenones

INVENTOR(S): Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042261	A2	20020530	WO 2001-US42939	20011114
WO 2002042261	A3	20030306		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002028593	A5	20020603	AU 2002-28593		20011114
PRIORITY APPLN. INFO.:			US 2000-253073P	P	20001127
			WO 2001-US42939	W	20011114

OTHER SOURCE(S): CASREACT 136:401533; MARPAT 136:401533

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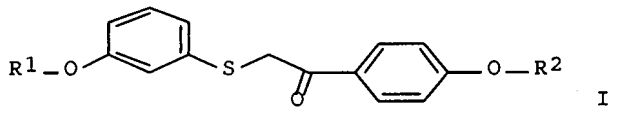

I

AB α-(3-Arylthio)acetophenones [I; R1, R2 = H, hydroxy-protecting group; e.g., α-(3-methoxyphenylthio)-4-methoxyacetophenone] are prepared in high yield and selectivity by the coupling of a thiophenol derivative 3-(R1O)C6H4SH (e.g., 3-methoxybenzenethiol) in an aqueous alkaline (e.g., KOH) solvent (e.g., Et acetate) with an aromatic ketone LCH2COC6H4(OR2)-4 (L = leaving group; e.g., α-chloro-4-methoxyacetophenone).

L3 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:283971 CAPLUS Full-text
DOCUMENT NUMBER:	134:300772
TITLE:	Glycosides and orthoester glycosides of raloxifene and analogues and the use thereof
INVENTOR(S):	Holick, Michael Francis; Ramanathan, Halasya
PATENT ASSIGNEE(S):	Strakan Group PLC, UK
SOURCE:	PCT Int. Appl., 28 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027129	A1	20010419	WO 2000-GB3864	20001006

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 2355007	A	20010411	GB 1999-28100		19991126
PRIORITY APPLN. INFO.:			US 1999-158141P	P	19991008
			US 2000-231573P	P	20000911

OTHER SOURCE(S): MARPAT 134:300772

AB Raloxifene and raloxifene analog glycosides and orthoester glycosides afford greater serum bioavailability of the hydroxylated parent compound, and are useful for treating or preventing a number of conditions that may be treated with an anti-estrogenic or an anti-androgenic compound To a mixture of 0.5 g

raloxifene and 1.6 g silver silicate in dry acetonitrile was added 3 g mol. sieves and stirred for 20 min. To the above suspension was added 1.0 g acetobromo-α-D-glucose and heated for 2 h at 60°, then filtered through a bed of silica gel and eluted with dichloromethane and methanol. The yellow eluent was concentrated under vacuum to obtain yellowish crystals. Proton NMR spectrum showed the crystals were consisted of 2 possible monoglucosides and a doubly glycosylated product.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:440767 CAPLUS Full-text
DOCUMENT NUMBER: 131:228604
TITLE: Synergistic methodologies for the synthesis of 3-aroyl-2-arylbenzo[b]thiophene-based selective estrogen receptor modulators. Two concise syntheses of raloxifene
AUTHOR(S): Bradley, David A.; Godfrey, Alexander G.; Schmid, Christopher R.
CORPORATE SOURCE: Chemical Process Research and Development, A Division of Eli Lilly and Company, Lilly Corporate Center, Lilly Research Laboratories, Indianapolis, IN, 46285-4813, USA
SOURCE: Tetrahedron Letters (1999), 40(28), 5155-5159
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Functionalized benzo[b]thiophene intermediates are prepd. which allow fully independent elaboration of the 2-aryl position or the tether position of benzo[b]thiophene-based selective estrogen receptor modulators (SERMs). Two concise syntheses of the SERM raloxifene (Evista) are presented.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:188589 CAPLUS Full-text
DOCUMENT NUMBER: 130:311683
TITLE: Novel nonsteroidal selective estrogen receptor modulators. Carbon and heteroatom replacement of oxygen in the ethoxypiperidine region of raloxifene
AUTHOR(S): Schmid, Christopher R.; Sluka, James P.; Duke, Kristen M.; Glasebrook, Andrew W.
CORPORATE SOURCE: Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(4), 523-528
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Compds. were synthesized where oxygen in the ethoxypiperidine region of raloxifene is replaced with carbon, sulfur, or nitrogen linkages. Thia- and aza-substituted compds. were prepared by novel methodol. The compds. were evaluated in vitro as selective estrogen receptor modulators (SERMs). Calcns. suggested the compds. exhibit an ER-α binding affinity/conformational energy relationship.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:71534 CAPLUS Full-text
DOCUMENT NUMBER: 130:196550
TITLE: Nucleophilic aromatic substitution on 3-aroyl-2-arylbenzothiophenes. Rapid access to raloxifene and other selective estrogen receptor modulators
AUTHOR(S): Schmid, Christopher R.; Sluka, James P.; Duke, Kristin M.
CORPORATE SOURCE: Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285-4813, USA
SOURCE: Tetrahedron Letters (1999), 40(4), 675-678
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:196550
AB Versatile, mild and high yielding methods for nucleophilic arom. substitution of 2-dialkylamino-1-ethoxides and related nucleophiles on 3-aroyl-2-arylbenzothiophene nuclei are presented. A short synthesis of raloxifene is detailed.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:721690 CAPLUS Full-text
DOCUMENT NUMBER: 130:3769
TITLE: Processes for preparing benzothiophenes
INVENTOR(S): McGill, John McNeil, III; Misner, Jerry Wayne; Zhang, Tony Yantao
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849156	A1	19981105	WO 1998-US8509	19980428
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2287943	A1	19981105	CA 1998-2287943	19980428
AU 9872613	A	19981124	AU 1998-72613	19980428
BR 9809439	A	20000613	BR 1998-9439	19980428
HU 200003187	A2	20010528	HU 2000-3187	19980428
JP 2001522372	T	20011113	JP 1998-547277	19980428
US 6090949	A	20000718	US 1998-69497	19980429
EP 875510	A1	19981104	EP 1998-303374	19980430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
MX 9909883	A	20000331	MX 1999-9883	19991027
PRIORITY APPLN. INFO.:			US 1997-45177P P	19970430

WO 1998-US8509 W 19980428
OTHER SOURCE(S): CASREACT 130:3769; MARPAT 130:3769
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y = Cl, Br, I, SO2(C1-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = C1-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:721501 CAPLUS Full-text
DOCUMENT NUMBER: 130:3768
TITLE: Demethylation process for preparing benzo[b]thiophenes
INVENTOR(S): Hoard, David Warren; Luke, Wayne Douglas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 875511	A1	19981104	EP 1998-303345	19980429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2236254	A1	19981030	CA 1998-2236254	19980427
JP 11005789	A	19990112	JP 1998-118628	19980428
US 5994547	A	19991130	US 1998-69500	19980429

PRIORITY APPLN. INFO.: US 1997-45156P P 19970430
OTHER SOURCE(S): CASREACT 130:3768; MARPAT 130:3768
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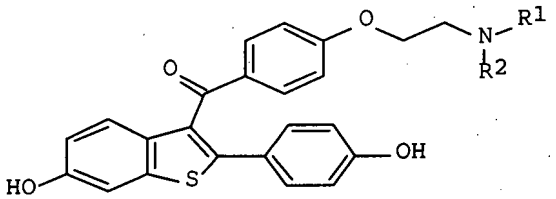
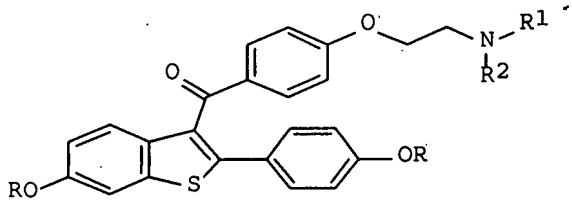


I



II

AB The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2-methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be carried out in the same reaction vessel without isolation of the acylated, protected material.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:719257 CAPLUS Full-text
DOCUMENT NUMBER: 130:3765
TITLE: Intermediates and processes for preparing benzo[b]thiophenes
INVENTOR(S): Misner, Jerry Wayne; Schmid, Christopher Randall
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848793	A1	19981105	WO 1998-US8510	19980428
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2287922	A1	19981105	CA 1998-2287922	19980428
AU 9872614	A	19981124	AU 1998-72614	19980428
EP 979076	A1	20000216	EP 1998-919936	19980428
R: AT, BE, DE, DK, ES, FR, GB, GR, IT, NL, SE, PT, IE, FI				
JP 2001523253	T	20011120	JP 1998-547278	19980428
US 6018056	A	20000125	US 1998-69278	19980429

PRIORITY APPLN. INFO.: US 1997-45131P P 19970430
WO 1998-US8510 W 19980428

OTHER SOURCE(S): CASREACT 130:3765; MARPAT 130:3765

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I-III; R = hydroxy protecting group; Y = CO2H, CO2(C1-4 alkyl), C(halo), etc.; A = OH, halo, NO2, etc.; R1 = hydroxy protecting group, H], useful intermediates in the further preparation of pharmaceutical benzo[b]thiophenes, were prepared Thus, reaction of 6-methoxythianaphthen-2-one with p-anisaldehyde in the presence of piperidine in EtOH and THF afforded 45% E/Z-I [R = Me].

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:161136 CAPLUS Full-text
DOCUMENT NUMBER: 128:221639
TITLE: Preparation of amorphous benzothiophenes for pharmaceuticals
INVENTOR(S): Cuff, George W.; Thakkar, Arvind L.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Cuff, George W.; Thakkar, Arvind L.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808513	A1	19980305	WO 1997-US14768	19970822
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 826682	A1	19980304	EP 1997-306426	19970822
EP 826682	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2263175	A1	19980305	CA 1997-2263175	19970822
AU 9742335	A	19980319	AU 1997-42335	19970822
AU 723987	B2	20000907		
IN 182940	A1	19990814	IN 1997-CA1549	19970822
BR 9713176	A	20000208	BR 1997-13176	19970822
CN 1244124	A	20000209	CN 1997-197434	19970822
HU 200001172	A2	20010628	HU 2000-1172	19970822
HU 200001172	A3	20020128		
NZ 333839	A	20010629	NZ 1997-333839	19970822
IL 128641	A	20011031	IL 1997-128641	19970822
TR 9900403	T2	20020121	TR 1999-403	19970822
JP 2002514174	T	20020514	JP 1998-511744	19970822
AT 234295	T	20030315	AT 1997-306426	19970822

ES 2195089	T3	20031201	ES 1997-306426		19970822
ZA 9707617	A	19990225	ZA 1997-7617		19970825
US 6713494	B1	20040330	US 1997-918741		19970825
NO 9900914	A	19990225	NO 1999-914		19990225
KR 2000035941	A	20000626	KR 1999-701682		19990227
PRIORITY APPLN. INFO.:			US 1996-24831P	P	19960828
			WO 1997-US14768	W	19970822

OTHER SOURCE(S): MARPAT 128:221639

AB A method for prepg. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:589698 CAPLUS Full-text

DOCUMENT NUMBER: 127:272904

TITLE: Evaluation of piperidinoethoxy moiety as an antiestrogenic substituent in non-steroidal anti-estrogens: fertility regulation

AUTHOR(S): Tripathi, Sachi; Dwivedy, Indra; Dhar, J. D.; Dwivedy, Anila; Ray, Suprabhat

CORPORATE SOURCE: Medicinal Chemistry Division, Central Drug Research Institute, Lucknow, 226 001, India

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(16), 2131-2136
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A piperidinoethoxy substituent in non-steroidal antiestrogens has a relatively higher antiestrogenic effect as compared to a pyrrolidinoethoxy moiety. However, the antagonistic activity is more depended on the mol. geometry than the nature of the basic chain. No significant difference in the antifertility activity in these two sets of compds. was observed

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:124440 CAPLUS Full-text

DOCUMENT NUMBER: 126:144105

TITLE: Preparation of 3-phenylbenzo[b]thiophenes

INVENTOR(S): Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Hoard, David W.; Luke, Wayne D.

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

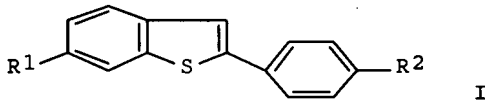
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640677	A1	19961219	WO 1996-US9477	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,				

ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

US 5606075	A	19970225	US 1995-481015		19950607
CA 2223709	A1	19961219	CA 1996-2223709		19960604
AU 9661010	A	19961230	AU 1996-61010		19960604
AU 703017	B2	19990311			
EP 830355	A1	19980325	EP 1996-918320		19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
CN 1192738	A	19980909	CN 1996-196109		19960604
BR 9608851	A	19990608	BR 1996-8851		19960604
JP 11507347	T	19990629	JP 1996-501787		19960604
HU 9900898	A2	19990728	HU 1999-898		19960604
HU 9900898	A3	20000228			
EP 1092714	A2	20010418	EP 2000-128207		19960604
EP 1092714	A3	20010704			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
IL 122128	A	20010808	IL 1996-122128		19960604
NO 9705627	A	19980127	NO 1997-5627		19971204
PRIORITY APPLN. INFO.:			US 1995-481015	A	19950607
			EP 1996-918320	A3	19960604
			WO 1996-US9477	W	19960604

OTHER SOURCE(S): MARPAT 126:144105
GI



I

AB Title compds. [I; R1,R2 = H, halo, (aryl)alkoxy, NH2] were pred. by cyclization of 4-R1C6H4CH:C(SR4)C6H4R2-4 [R4 = trialkylsilyloxy, (di)(alkyl)amino, alkylthio, etc.] in the presence of an acid.

L3 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:740256 CAPLUS Full-text
DOCUMENT NUMBER: 126:7985
TITLE: Preparation of 3-[4-(2-heterocyclylethoxy)benzoyl-2-phenylbenzothiophenes for use in alleviating the symptoms of post-menopausal syndrome
INVENTOR(S): Dodge, Jeffrey Alan; Jones, Charles David; Bourgeois, Tokarz Michelle Lee
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 67 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 738725	A2	19961023	EP 1996-302713	19960418
EP 738725	A3	19970305		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, NL, PT, SE				
US 6608090	B1	20030819	US 1995-426552	19950421
CA 2215902	A1	19961024	CA 1996-2215902	19960418
WO 9632937	A1	19961024	WO 1996-US5382	19960418
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9655549	A	19961107	AU 1996-55549	19960418
JP 11504013	T	19990406	JP 1996-531911	19960418
PRIORITY APPLN. INFO.:			US 1995-426339 A	19950421
			US 1995-426552 A	19950421
			WO 1996-US5382 W	19960418

OTHER SOURCE(S): MARPAT 126:7985

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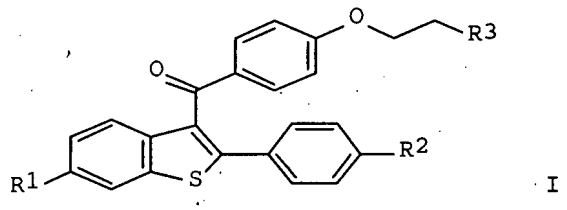

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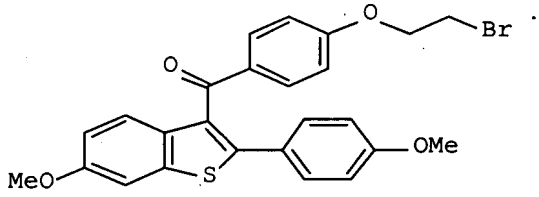

II

AB The title compds. [I; R1, R2 = H, OH, alkoxy, etc.; R3 = (substituted) pyrrolidino, piperidino, piperazino, etc.], useful in alleviating the symptoms of post-menopausal syndrome related to osteoporosis, cardiovascular disease, hyperlipidemia, estrogen-dependent cancer, and in alleviating the symptoms of uterine fibroid disease, endometriosis, aortal smooth muscle cell proliferation, and restenosis, were prepared and formulated. Thus, reaction of bromide II with 3-phenylpyrrolidine in DMF followed by demethylation with EtSH/AlCl3 in CH2Cl2 afforded I [R1, R2 = H; R3 = 3-Ph-pyrrolidin-1-yl] which reduced 63.4% serum cholesterol at 10 mg/kg.

L3 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:672963 CAPLUS Full-text

DOCUMENT NUMBER: 126:7983

TITLE: Process for the synthesis of benzo[b]thiophenes

INVENTOR(S): Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: U.S., 10 pp.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5569772	A	19961029	US 1995-486873	19950607
CA 2223681	A1	19961219	CA 1996-2223681	19960604
WO 9640678	A1	19961219	WO 1996-US9357	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9660970	A	19961230	AU 1996-60970	19960604
AU 698558	B2	19981029		
EP 830356	A1	19980325	EP 1996-918277	19960604
EP 830356	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192212	A	19980902	CN 1996-195899	19960604
BR 9609156	A	19990629	BR 1996-9156	19960604
JP 11507338	T	19990629	JP 1997-501694	19960604
HU 9900903	A2	19990728	HU 1999-903	19960604
HU 9900903	A3	20010129		
IL 122091	A	20010520	IL 1996-122091	19960604
AT 204575	T	20010915	AT 1996-918277	19960604
ES 2159742	T3	20011016	ES 1996-918277	19960604
PT 830356	T	20011228	PT 1996-918277	19960604
NO 9705579	A	19971203	NO 1997-5579	19971203
PRIORITY APPLN. INFO.:			US 1995-486873 A	19950607
			WO 1996-US9357 W	19960604

OTHER SOURCE(S): CASREACT 126:7983; MARPAT 126:7983
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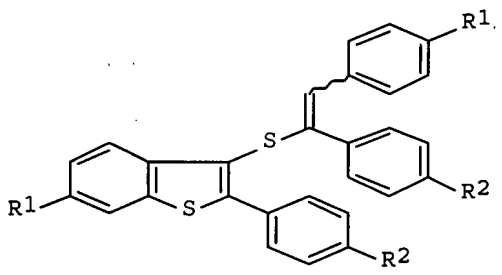

I

AB The title compds. I [R1, R2 = H, alkoxy, etc.] are prepd. Thus, treatment of (E)-tert-Bu 4,4'-dimethoxystilbenyl sulfoxide with p-toluenesulfonic acid in refluxing toluene gave, after workup and purifn, (E)- and (Z)-I [R1 = R2 = MeO].

L3 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:649600 CAPLUS Full-text
DOCUMENT NUMBER: 125:266032
TITLE: Phosphorous-containing benzothiophenes, their preparation, their use in treating postmenopausal syndrome-associated indications and estrogen-dependent diseases, and pharmaceuticals containing them
INVENTOR(S): Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey S.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 729964	A1	19960904	EP 1996-300878	19960209
EP 729964	B1	20010509		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 6479517	B1	20021112	US 1995-395944	19950228
ES 2158242	T3	20010901	ES 1996-300878	19960209
CA 2169414	A1	19960829	CA 1996-2169414	19960213
JP 08259560	A	19961008	JP 1996-25281	19960213
US 5998443	A	19991207	US 1997-946842	19971008
PRIORITY APPLN. INFO.:			US 1995-395944 A	19950228
OTHER SOURCE(S):	MARPAT 125:266032			

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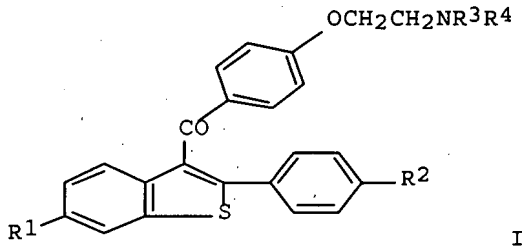

I

AB Phosphorus-contg. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(O-alkyl)2, OPO(O-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3-dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds.

of the invention, as well as pharmaceutical compns. containing compds. of the invention.

L3 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:333087 CAPLUS Full-text
DOCUMENT NUMBER: 125:86485
TITLE: Prepn. of vinyl sulfenic acid derivatives for benzo[b]thiophene synthesis
INVENTOR(S): Hoard, David W.; Luke, Wayne D.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5514826	A	19960507	US 1995-483607	19950607
CA 2224225	A1	19961219	CA 1996-2224225	19960604
WO 9640693	A1	19961219	WO 1996-US9460	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
AU 9661003	A	19961230	AU 1996-61003	19960604
AU 698076	B2	19981022		
EP 830362	A1	19980325	EP 1996-918314	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192215	A	19980902	CN 1996-195947	19960604
CN 1068883	B	20010725		
BR 9608847	A	19990608	BR 1996-8847	19960604
JP 11507346	T	19990629	JP 1997-501774	19960604
HU 9900923	A2	19990728	HU 1999-923	19960604
HU 9900923	A3	20000228		
IL 122127	A	20010520	IL 1996-122127	19960604
NO 9705633	A	19980128	NO 1997-5633	19971204
CN 1330071	A	20020109	CN 2000-130796	20001212

PRIORITY APPLN. INFO.:

US 1995-482692	A	19950607
US 1995-483607	A	19950607
WO 1996-US9460	W	19960604

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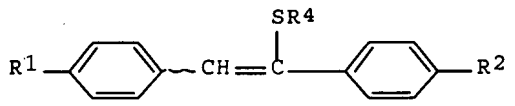

I

AB The present invention is directed to novel vinyl sulfenic acid derivs. I [R1, R2 = H, alkoxy, arylalkoxy, halo, amino; R4 = OSi(R3)3, NR5R6, SR8; R5and/or R6 = H, alkyl, arylalkyl, aryl, -(CH2)5-, -(CH2)4-, -(CH2)2O(CH2)2-, -(CH2)6-;

R8 = alkyl, aryl, arylalky] useful for the synthesis of benzo[b]thiophenes, in particular 2-arylbenzo[b]thiophenes. E.g., desoxyanisoin reacts with 2-methyl-2-propanethiol to give I [R1 = R2 = OMe; R4 = C(Me)3] which in turn cyclizes to 6-methoxy-2-(4- methoxyphenyl)benzo[b]thiophene.

L3 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:256454 CAPLUS Full-text
DOCUMENT NUMBER: 124:289252
TITLE: Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceutical agents
INVENTOR(S): Kjell, Douglas Patton
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 699673	A1	19960306	EP 1995-306053	19950830
EP 699673	B1	19980422		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5731436	A	19980324	US 1994-298891	19940831
IL 115091	A	20000831	IL 1995-115091	19950828
IL 126593	A	20000831	IL 1995-126593	19950828
CA 2157235	A1	19960301	CA 1995-2157235	19950830
FI 9504068	A	19960301	FI 1995-4068	19950830
HU 73136	A2	19960628	HU 1995-2539	19950830
BR 9503847	A	19960917	BR 1995-3847	19950830
AT 165356	T	19980515	AT 1995-306053	19950830
ES 2114722	T3	19980601	ES 1995-306053	19950830
JP 08119912	A	19960514	JP 1995-223184	19950831
US 5955608	A	19990921	US 1998-16761	19980130
PRIORITY APPLN. INFO.:			US 1994-298891 A	19940831
			IL 1995-115091 A3	19950828

OTHER SOURCE(S): MARPAT 124:289252
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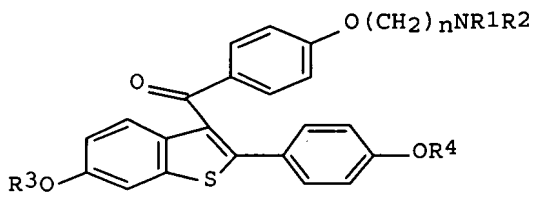

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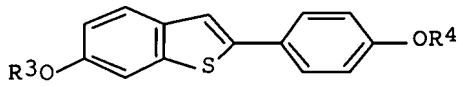

II

AB The present invention provides a novel process for prepg. a compd. of formula RO2C(p-C6H4)O(CH2)nNR1R2 [R = C1-C4 alkyl; R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino,

morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3]; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2(p-C6H4)O(CH2)nOH [R and n are as defined above, with a leaving group donor]; and (c) reacting the product of step (b), a compound of formula RO2(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneamine]. The product of the above process also is novel and is useful for the preparation of pharmaceutically active compds. of formula I, particularly via the following novel process [R = C1-C4 alkyl; R1 and R2 each are independently C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino, morpholino, dimethylamino, diethylamino, of 1-hexamethyleneimino; n = 2, 3]; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2C(p-C6H4)O(CH2)nOH [R and n are as defined above, with the leaving group donor]; (c) reacting the product of step (b), a compound of formula RO2C(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneimine]; (d) reacting the product of step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing the reaction product from step (d); and (f) optionally forming a salt of the reaction product from either step (d) or step (e).

L3 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:237478 CAPLUS Full-text
DOCUMENT NUMBER: 124:289249
TITLE: An improved process for preparing 3-(4-aminoethoxybenzoyl)benzo[b]thiophenes
INVENTOR(S): Alt, Charles Arthur
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 693488	A1	19960124	EP 1995-305085	19950720
EP 693488	B1	20010919		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5523416	A	19960604	US 1995-422294	19950414
HU 71596	A2	19960129	HU 1995-2176	19950719
AU 9525068	A	19960201	AU 1995-25068	19950719
AU 684181	B2	19971204		
ZA 9506031	A	19970120	ZA 1995-6031	19950719
CA 2154319	A1	19960123	CA 1995-2154319	19950720
FI 9503513	A	19960123	FI 1995-3513	19950720
NO 9502891	A	19960123	NO 1995-2891	19950720
CN 1116624	A	19960214	CN 1995-109618	19950720

JP 08053440	A	19960227	JP 1995-183923		19950720
IL 114684	A	19990620	IL 1995-114684		19950720
AT 205842	T	20011015	AT 1995-305085		19950720
ES 2160668	T3	20011116	ES 1995-305085		19950720
PT 693488	T	20020228	PT 1995-305085		19950720
BR 9503408	A	19960227	BR 1995-3408		19950721
US 5512684	A	19960430	US 1995-512724		19950808
PRIORITY APPLN. INFO.:			US 1994-279456	A	19940722
			US 1995-422294	A1	19950414

OTHER SOURCE(S): CASREACT 124:289249; MARPAT 124:289249

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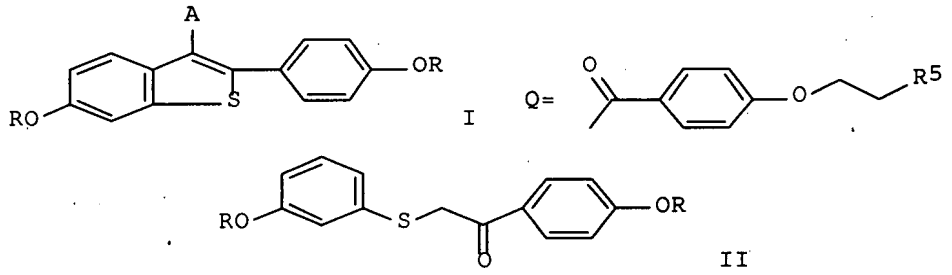
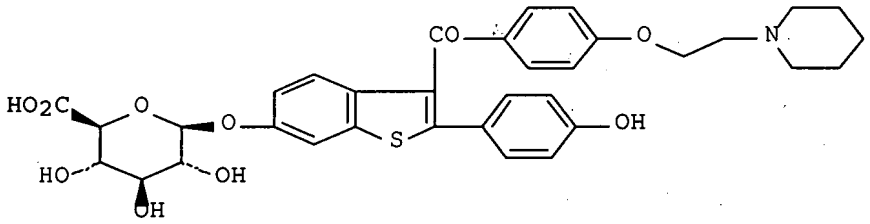


AB A process for prepg. 6-alkoxy-3-(4-alkoxyphenyl)benzo[b]thiophenes (I; A = H; R = same or different C1-6 alkyl) in good yield on a manufacturing scale without generating a thick, potentially yield-reducing, paste and thereby without mixing problems, involves intramol. cyclization of α-(3-alkoxyphenylthio)-4-alkoxyacetophenones (II; R = same as above). The invention also provides methods for converting α-(alkoxyphenylthio)-4-alkoxyacetophenones I (A = H; R = same as above) into 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2- aminoethoxy)benzoyl]benzo[B]thiophenes I (A = Q, R = H; R5 = NR1R2; wherein R1, R2 = C1-4 alkyl, or R1R2 = C4-6 polymethylene or CH2CH2OCH2CH2) via acylation of a dialkoxy benzo[b]thiophene I (A = H; R = same as above) with an acylating agent R4-Q (R4 = Cl, Br, an active ester, etc.; R5 = same as above) under Friedel-Crafts conditions. Thus, 164 g α-bromo-4-methoxyacetophenone was added portion-wise to a mixture of 100 g 4-methoxybenzenethiol and 39 g KOH in 300 mL and denatured EtOH in a cooling and stirred for 10 min in the cooling bath and at ambient temperature for 3 h to give, after workup, 158 g α-(3-methoxyphenylthio)-4- methoxyacetophenone. The latter compound (6.92 g) was added steadily over 1/2 h to a mixture of 41.5 g polyphosphoric acid and 13.8 g phosphoric acid and the reaction mixture was heated at 85° for 1.75 h and cooled to 50°, to give , after extraction with toluene and crystallization, the desired 6-isomer, I (A = H, R = Me)(69% yield). The latter compound (30 g) was heated with 90 g pyridine hydrochloride with stirring at 210° for 30 min to give, after workup, 25.5 g I (A = R = H), which (40 g) was acetylated by Ac2O in the presence of 4-dimethylaminopyridine in pyridine to give 52.5 g I (A = H, R = Ac). This compound (20 g) was added to a solution of 4-(2-piperidinoethoxy)benzoyl chloride (prepared from 16.3 g of the benzoic acid derivative) in ClCH2CH2Cl and stirred vigorously, followed by adding 73.4 g AlCl3 over 3 min, and the resulting mixture was stirred for 1 h to give, after workup, the desired product I [A = Q (wherein R5 = piperidino), R = Ac] as an oil, which was saponified with a mixture of 275 mL MeOH and 55 mL 5 n aqueous NaOH under reflux to give 10.5 g the title compound I [A = Q, wherein R5 = piperidino, R = H].

L3 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:150242 CAPLUS Full-text
DOCUMENT NUMBER: 124:202950
TITLE: Preparation of benzothiophene glucopyranosides as antihyperlipidemics.
INVENTOR(S): Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom, Terry Donald; Lugar, Charles Willis Iii; Staten, Gilbert Stanley
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 683170	A1	19951122	EP 1995-303265	19950516
EP 683170	B1	19990922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5567820	A	19961022	US 1995-404701	19950315
US 6723739	B1	20040420	US 1995-405555	19950315
CA 2149501	A1	19951121	CA 1995-2149501	19950516
ZA 9503975	A	19961118	ZA 1995-3975	19950516
AT 184880	T	19991015	AT 1995-303265	19950516
ES 2136799	T3	19991201	ES 1995-303265	19950516
AU 9520121	A	19951130	AU 1995-20121	19950517
AU 683734	B2	19971120		
JP 07316180	A	19951205	JP 1995-118338	19950517
FI 9502420	A	19951121	FI 1995-2420	19950518
NO 9501954	A	19951121	NO 1995-1954	19950518
NO 304686	B1	19990201		
CN 1116626	A	19960214	CN 1995-106322	19950518
CN 1039013	B	19980708		
BR 9502079	A	19960305	BR 1995-2079	19950518
HU 73788	A2	19960930	HU 1995-1466	19950518
HU 219335	B	20010328		
IL 113780	A	19990620	IL 1995-113780	19950518
GR 3032142	T3	20000427	GR 1999-403228	19991215
US 2004167080	A1	20040826	US 2004-778865	20040212
PRIORITY APPLN. INFO.:			US 1994-246655 A	19940520
			US 1995-405555 A1	19950315

OTHER SOURCE(S): CASREACT 124:202950
GI



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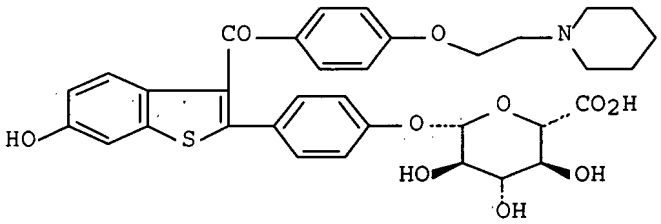

II

AB Raloxifene metabolites (I) and (II) and their hydrochloride salts were prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-O-tetraacetyl-D-glucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

L3 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:123714 CAPLUS Full-text
DOCUMENT NUMBER: 124:155994
TITLE: Pharmaceutical compositions containing 2-phenyl-3-aryoylbenzothiophenes for for inhibiting bone loss and lowering serum cholesterol
INVENTOR(S): Draper, Michael W.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Can. Pat. Appl., 31 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2141999	A1	19950903	CA 1995-2141999	19950207
US 5478847	A	19951226	US 1994-205012	19940302
ZA 9500976	A	19960807	ZA 1995-976	19950207
NZ 314699	A	20000728	NZ 1995-314699	19950207
EP 674903	A1	19951004	EP 1995-300842	19950210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9500774	A	19950904	NO 1995-774	19950228
RU 2100024	C1	19971227	RU 1995-102778	19950228
RU 2150275	C1	20000610	RU 1996-119781	19950228
AU 9513551	A	19950907	AU 1995-13551	19950301
AU 702575	B2	19990225		
JP 07267861	A	19951017	JP 1995-41769	19950301
JP 2818384	B2	19981030		
BR 9500784	A	19951024	BR 1995-784	19950301
CN 1119530	A	19960403	CN 1995-100021	19950301

HU 72638	A2	19960528	HU 1995-634		19950301
JP 10291932	A	19981104	JP 1998-107550		19950301
JP 10310525	A	19981124	JP 1998-107549		19950301
US 5610168	A	19970311	US 1995-422289		19950414
US 5641790	A	19970624	US 1995-422417		19950414
US 5747510	A	19980505	US 1997-788984		19970127
US 39050	E1	20060328	US 2003-375274		20030227
PRIORITY APPLN. INFO.:			US 1994-205012	A	19940302
			JP 1995-41769	A3	19950301
			US 1995-422417	A1	19950414

AB A method of inhibiting bone loss or resorption, or lowering serum cholesterol, comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in post-menopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

L3 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:991025 CAPLUS Full-text
DOCUMENT NUMBER: 124:106673
TITLE: Methods for lowering serum cholesterol
INVENTOR(S): Black, Larry J.; Bryant, Henry U.; Cullinan, George J.; Kauffman, Raymond F.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5464845	A	19951107	US 1993-159159		19931130
TW 383306	B	20000301	TW 1993-82100751		19930204
RU 2123335	C1	19981220	RU 1993-55026		19931213
ZA 9309427	A	19950615	ZA 1993-9427		19931215
SK 279271	B6	19980805	SK 1993-1421		19931215
IL 108042	A	19980104	IL 1993-108042		19931216
CZ 283863	B6	19980617	CZ 1993-2790		19931216
HU 69686	A2	19950928	HU 1993-3676		19931220
HU 223342	B1	20040628			
RO 113806	B1	19981130	RO 1993-1739		19931220
PL 177349	B1	19991029	PL 1993-301579		19931220
CA 2112017	A1	19940623	CA 1993-2112017		19931221
CA 2112017	C	20050614			
NO 9304740	A	19940623	NO 1993-4740		19931221
AU 9352578	A	19940707	AU 1993-52578		19931221
AU 669235	B2	19960530			
BR 9305182	A	19940816	BR 1993-5182		19931221
JP 06234632	A	19940823	JP 1993-323825		19931222
JP 3197129	B2	20010813			
CN 1094042	A	19941026	CN 1993-121277		19931222
CN 1043608	B	19990616			
AT 233559	T	20030315	AT 1993-310438		19931222
ES 2193142	T3	20031101	ES 1993-310438		19931222
PRIORITY APPLN. INFO.:			US 1992-995222	B2	19921222

OTHER SOURCE(S): MARPAT 124:106673
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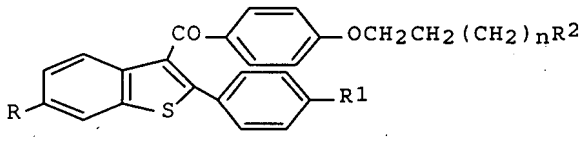


I

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof. The tested compds. lowered LDL without significantly affecting primary sex targets.

L3 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:362913 CAPLUS Full-text
DOCUMENT NUMBER: 122:213884
TITLE: A chemical probe for the estrogen receptor: synthesis of the 3H-isotopomer of raloxifene
AUTHOR(S): Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C. David
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (1995), 36(1), 43-9
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate was accessed by regioselective aroylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1-piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me ethers in the presence of the ethoxy side-chain followed by palladium catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

L3 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:700754 CAPLUS Full-text
DOCUMENT NUMBER: 121:300754
TITLE: [[(Alkylsulfonyl)oxy]benzo[b]thienyl]methanones and [[(aminocarbonyl)oxy]benzo[b]thienyl]methanones pharmaceuticals
INVENTOR(S): Black, Larry John; Bryant, Henry Uhlman; Cullinan, George Joseph
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 26 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 617030	A1	19940928	EP 1994-301871		19940316
EP 617030	B1	19990526			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
US 5482949	A	19960109	US 1993-35121		19930319
ZA 9401786	A	19950914	ZA 1994-1786		19940314
CA 2119091	A1	19940920	CA 1994-2119091		19940315
NO 9400940	A	19940920	NO 1994-940		19940316
AU 9457863	A	19940922	AU 1994-57863		19940316
AU 670177	B2	19960704			
BR 9401183	A	19941101	BR 1994-1183		19940316
HU 70549	A2	19951030	HU 1994-774		19940316
AT 180479	T	19990615	AT 1994-301871		19940316
ES 2132339	T3	19990816	ES 1994-301871		19940316
FI 9401262	A	19940920	FI 1994-1262		19940317
JP 06321937	A	19941122	JP 1994-47091		19940317
CN 1097420	A	19950118	CN 1994-102910		19940317
US 5994371	A	19991130	US 1995-392445		19950222
US 5599833	A	19970204	US 1996-588670		19960117
US 5605924	A	19970225	US 1996-588663		19960117
US 5798351	A	19980825	US 1997-958535		19971027
PRIORITY APPLN. INFO.:			US 1993-35121	A	19930319
			US 1995-392445	A3	19950222

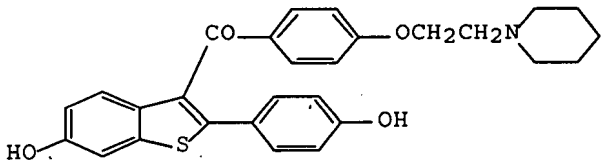
OTHER SOURCE(S): MARPAT 121:300754
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The (4-alkoxybenzoyl)benzo[b]thiophene-6-sulfonates and (4-alkoxybenzoyl)benzo[b]thien-6-yl carbamates I (R = OH, alkoxysulfonyl, carbamoyl; R1 = H, OH, halo, etc.; R2 = pyrrolidino, piperidino, etc.; X = bond, methine) were disclosed as agents for inhibiting the loss of bone, lowering serum cholesterol levels and therapeutically treating hormone dependent mammalian breast and uterine carcinoma. A specifically claimed example compound is [6-[(pentylsulfonyl)oxy]-2-[4-[(pentylsulfonyl)oxy]phenyl]benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone (II).

L3 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:448784 CAPLUS Full-text
DOCUMENT NUMBER: 101:48784
TITLE: Antiestrogens. 2. Structure-activity studies in a series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone hydrochloride (LY 156758), a remarkably effective estrogen antagonist with only minimal intrinsic estrogenicity
AUTHOR(S): Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.;

Peters, Mary K.; Black, Larry J.; Thompson, Allen R.; Falcone, Julie F.; Clemens, James A.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Medicinal Chemistry (1984), 27(8), 1057-66
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB In an effort to prep. nonsteroidal antiestrogens demonstrating greater antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b]thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino)ethoxy side chain functionality elsewhere in the mol. was AlCl3/EtSH. The benzothiophene derivs. were tested for their ability to inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1- piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. In antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

L3 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:156501 CAPLUS Full-text
DOCUMENT NUMBER: 100:156501
TITLE: Antiestrogenic and antiandrogenic benzothiophenes
INVENTOR(S): Jones, Charles D.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4418068	A	19831129	US 1981-331042	19811216
ZA 8202247	A	19831130	ZA 1982-2247	19820401
PRIORITY APPLN. INFO.:			US 1981-246335 A2	19810403

OTHER SOURCE(S): CASREACT 100:156501

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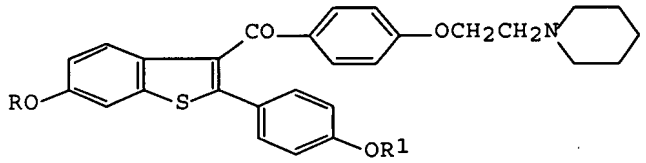

I

AB Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un)substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2-piperidinoethoxy)benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered 0.03 μg estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

L3 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:71917 CAPLUS Full-text

DOCUMENT NUMBER: 98:71917

TITLE: Benzothiophene compounds

INVENTOR(S): Jones, Charles David

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 107 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62503	A1	19821013	EP 1982-301737	19820401
R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8282265	A	19821007	AU 1982-82265	19820401
AU 555658	B2	19861002		
GB 2097788	A	19821110	GB 1982-9680	19820401
GB 2097788	B	19850424		
JP 57181081	A	19821108	JP 1982-56479	19820402
PRIORITY APPLN. INFO.:			US 1981-246335 A	19810403
			US 1981-331045 A	19811216

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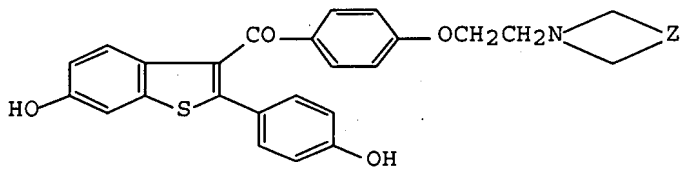

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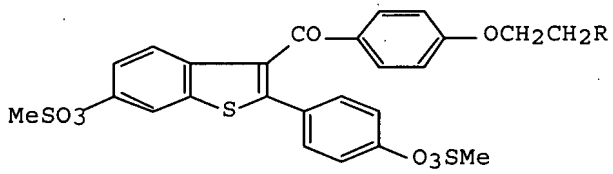

II

AB [(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were prepared, and limited the increase of uterine weight in rats treated with estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).

L3 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:71916 CAPLUS Full-text
DOCUMENT NUMBER: 98:71916
TITLE: 3-(4-Aminoethoxybenzoyl)benzo[b]thiophenes
INVENTOR(S): Jones, Charles David; Goettel, Mary Elizabeth
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62504	A1	19821013	EP 1982-301738	19820401
EP 62504	B1	19860102		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4358593	A	19821109	US 1981-246334	19810403
IL 65378	A	19860228	IL 1982-65378	19820330
CA 1167037	A1	19840508	CA 1982-400300	19820331
GB 2097392	A	19821103	GB 1982-9679	19820401
GB 2097392	B	19850424		
DD 201793	A5	19830810	DD 1982-238654	19820401
CS 227348	B2	19840416	CS 1982-2357	19820401
PL 130867	B1	19840929	PL 1982-235752	19820401
AT 17243	T	19860115	AT 1982-301738	19820401
DK 8201512	A	19821004	DK 1982-1512	19820402
FI 8201160	A	19821004	FI 1982-1160	19820402
JP 57183788	A	19821112	JP 1982-56480	19820402
ES 511124	A1	19830616	ES 1982-511124	19820402
HU 28787	A2	19831228	HU 1982-1026	19820402
HU 191353	B	19870227		
SU 1155157	A3	19850507	SU 1982-3417550	19820402

PRIORITY APPLN. INFO.:

US 1981-246334	A	19810403
US 1981-246335	A	19810403
US 1981-331045	A	19811216
EP 1982-301738	A	19820401

OTHER SOURCE(S): MARPAT 98:71916
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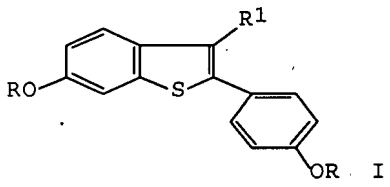

I

AB Benzothiophenes I [R = H; R1 = COC6H4O(CH2)2NR2R3-4; R2 = R3 = alkyl; R2R3 = (CH2)4-6, (CH2)2O(CH2)2, etc.] were prepared by Friedel-Crafts acylation of I (R = Ac, Bz, MeSO2; R1 = H) followed by hydrolysis of the ester groups. Thus, HSC6H4OMe-3 was treated with BrCH2COC6H4OMe-4 to give 3-MeOC6H4SCH2COC6H4OMe-4, which was cyclized with polyphosphoric acid to give I (R = Me, R1 = H). Demethylation of the latter followed by esterification with MeSO2Cl gave I (R = MeSO2, R1 = H; II). Friedel-Crafts acylation of 4 g II with 4-Me2N(CH2)2OC6H4COCl gave 6.2 g I [R = MeSO2, R1 = COC6H4O(CH2)2NMe2-4, III]. Hydrolysis of III gave I (R = H). I are estrogens, antiestrogens, and antiandrogens (no data).

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	115.67	124.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-30.42	-30.42

FILE 'REGISTRY' ENTERED AT 13:33:42 ON 21 AUG 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 AUG 2007 HIGHEST RN 945102-95-4
DICTIONARY FILE UPDATES: 20 AUG 2007 HIGHEST RN 945102-95-4

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http://www.cas.org/support/stngen/stndoc/properties.html

```
=> s e4
L4            1 "RALOXIFENE HYDROCHLORIDE"/CN

=> d l4 1 ide

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   82640-04-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-
     piperidinyl)ethoxy]phenyl]-, hydrochloride (1:1)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-
     piperidinyl)ethoxy]phenyl]-, hydrochloride (9CI)
OTHER NAMES:
CN   Bonebay
CN   Bontact
CN   Evista
CN   Fiona
CN   Keoxifene hydrochloride
CN   LY 156758
CN   Ralofen
CN   Raloxifene hydrochloride
CN   Reloxafine
MF   C28 H27 N O4 S . Cl H
CI   COM
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
       BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, CSCHEM, EMBASE, HSDB*,
       IMSPATENTS, IMSRESEARCH, IPA, MRCK*, MSDS-OHS, PATDPASPC, PHAR, PROMT,
       PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
CRN  (84449-90-1)
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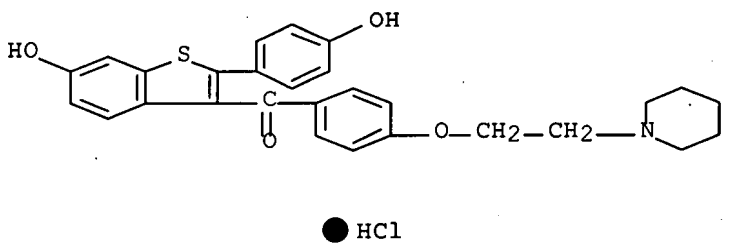


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

          329 REFERENCES IN FILE CA (1907 TO DATE)
            1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          329 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         8.25     132.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                         0.00     -30.42

FILE 'CAPLUS' ENTERED AT 13:35:36 ON 21 AUG 2007
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FILE COVERS 1907 - 21 Aug 2007  VOL 147 ISS 9
FILE LAST UPDATED: 20 Aug 2007  (20070820/ED)

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=> s l4
L5          329 L4

=> d scan

L5    329 ANSWERS   CAPLUS  COPYRIGHT 2007 ACS on STN
CC   63-6 (Pharmaceuticals)
TI   Preparation of raloxifene hydrochloride capsules and establishment of its
     quality control standard
ST   raloxifene hydrochloride capsules dissoln quality control
IT   Drug delivery systems
        (capsules; preparation of raloxifene hydrochloride capsules and
        establishment of quality control standard)
IT   Dissolution
     Quality control
        (preparation of raloxifene hydrochloride capsules and establishment of
        quality control standard)
IT   63-42-3, Lactose   9004-32-4, Carboxymethyl cellulose sodium   9004-34-6,
     Cellulose, biological studies
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (preparation of raloxifene hydrochloride capsules and establishment of
        quality control standard)
IT   82640-04-8, Raloxifene hydrochloride
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
```

(Uses)
(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 1
TI Effectiveness of combined GnRH analogue plus raloxifene administration in the treatment of uterine leiomyomas: a prospective, randomized, single-blind, placebo-controlled clinical trial
ST leuprolide acetate SERM raloxifene pelvic pain menorrhagia uterine leiomyomas
IT Human
(GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Intestine, disease
(constipation; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Menopause
(hot flash; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Uterus, neoplasm
(leiomyoma; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Menstrual disorder
(menorrhagia; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Body, anatomical
(pelvis, pain; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Menopause
(premenopause; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective modulator of; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Urinary system, disease
(urinary frequency; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT 74381-53-6, Leuprolide acetate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Enantone; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT **82640-04-8**, Raloxifene hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC ICM C07D333-64
ICS C07D333-56
CC 27-9 (Heterocyclic Compounds (One Hetero Atom))
TI Demethylation process for preparing benzo[b]thiophenes
ST demethylation benzothiophene benzenethiol
IT 63675-73-0P 63675-74-1P 84541-36-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(demethylation process for preparing benzo[b]thiophenes)
IT 63676-25-5P **82640-04-8P** 84449-87-6P 84449-90-1P
215662-11-6P 215662-12-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(demethylation process for preparing benzo[b]thiophenes)
IT 108-90-7, Chlorobenzene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(demethylation process for preparing benzo[b]thiophenes)
IT 2632-13-5 7340-90-1 7446-70-0, Aluminum chloride, reactions
15570-12-4, 3-Methoxybenzenethiol 84449-80-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(demethylation process for preparing benzo[b]thiophenes)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC ICM A61K031-445
ICS A61K031-40; A61K031-38
INCL 514324000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
TI Methods of decreasing serum calcium levels
ST benzoyl benzothiophene calcium blood decrease; raloxifene calcium blood decrease
IT **82640-04-8**, Raloxifene hydrochloride 84449-90-1, Raloxifene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzoylbenzothiophene derivs. for decreasing serum calcium levels)
IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoylbenzothiophene derivs. for decreasing serum calcium levels)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC C12Q001-02
INCL 435029000
CC 2-1 (Mammalian Hormones)
TI Cell culture for screening estrogen agonists and antagonists
ST estrogen agonist screening cell culture; antagonist estrogen screening cell culture
IT Animal cell line

(C7 MCF7-173, in screening of estrogen agonists/antagonists)
IT Estrogens
RL: ANST (Analytical study)
(agonists, cell culture method for screening of)
IT Cell proliferation
(cells dependent on estrogens for, in screening of estrogen agonists/antagonists)
IT Charcoal
RL: ANST (Analytical study)
(dextran-, human serum stripped with, for maintaining medium in cell culture method for screening of estrogen agonists/antagonists)
IT Blood serum
(fetal bovine, for maintaining medium in cell culture method for screening of estrogen agonists/antagonists)
IT Animal tissue culture
(for estrogen agonist/antagonist screening)
IT Proteins, biological studies
RL: BIOL (Biological study)
(inhibitory to proliferation of estrogen-dependent cells in vitro, for cell culture method for screeing of estrogen agonists/antagonists)
IT Estrogens
RL: PRP (Properties)
(antiestrogens, cell culture method for screening of)
IT Mammary gland
(neoplasm, cells of, in screening of estrogen agonists/antagonists)
IT 50-27-1, Estriol 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies
RL: ANST (Analytical study)
(agonists and antagonists of, cell culture method for screening of)
IT 9004-54-0, Dextran, biological studies
RL: BIOL (Biological study)
(charcoal-, human serum stripped with, for maintaining medium in cell culture method for screening of estrogen agonists/antagonists)
IT 10540-29-1, Tamoxifen 34816-55-2, Moxestrol 63676-25-5, LY117018 71794-60-0, 11β-Chloromethylestradiol 82640-04-8, LY156758 120382-04-9, RU39411 57-83-0, Progesterone, biological studies
RL: ANST (Analytical study)
(estrogen agonist/antagonist activity of, determination of, cell culture method for)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l4/prep
329 L4
4449106 PREP/RL
L6 34 L4/PREP
(L4 (L) PREP/RL)

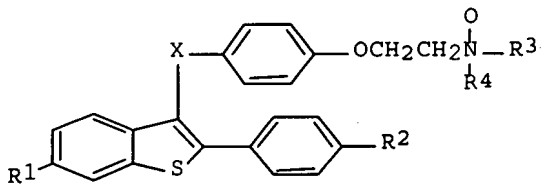
=> d l6 ibib abs 1-
YOU HAVE REQUESTED DATA FROM 34 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:265820 CAPLUS Full-text
DOCUMENT NUMBER: 146:448285
TITLE: Benzothiophenes, formulations containing same, and methods
INVENTOR(S): Cullinan, George J.; Palkowitz, Alan D.
PATENT ASSIGNEE(S): USA
SOURCE: Hung. Pat. Appl., 40pp.

CODEN: HUXXCV
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 9901882	A2	20000228	HU 1999-1882	19970219
HU 9901882	A3	20000328		

PRIORITY APPLN. INFO.: HU 1999-1882 19970219
OTHER SOURCE(S): MARPAT 146:448285
GI



I

AB Benzothiophene N-oxides I [R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, Cl or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-[2-(1- piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.

L6 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:958171 CAPLUS Full-text
DOCUMENT NUMBER: 147:9760
TITLE: Synthesis of raloxifene hydrochloride
AUTHOR(S): Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong, Ping
CORPORATE SOURCE: Shenyang Institute of Chemical Technology, Faculty of Pharmaceutical-Engineering, Shenyang, 110142, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2005), 14(7), 882-884
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3-methoxybenzenethiol and 4-methoxy-α-bromo acetophenone via five steps,

including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

L6 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1257978 CAPLUS Full-text
DOCUMENT NUMBER: 144:135192
TITLE: Manufacture of raloxifene-hydrochloride-containing medicines for treating bone fracture delayed union or nonunion
INVENTOR(S): Zhang, Jianhao; Huang, Haibo
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1615860	A	20050518	CN 2003-10113253	20031111
PRIORITY APPLN. INFO.:			CN 2003-10113253	20031111

AB The title medicines are manufd. from (by wt.) raloxifene hydrochloride (35-45%) as effective components, diluent (50-60%), disintegrant (2-4%), lubricant (0.5-1%), and adhesive (2-3%). The medicines can be produced into various drug forms such as tablets, capsules, suspensions, powders, granules, solns., etc., and have advantages of short course of treatment, high recovery rate, etc.

L6 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:547361 CAPLUS Full-text
DOCUMENT NUMBER: 143:59836
TITLE: A process for preparing benzoic acid derivatives, useful as intermediates for preparation of raloxifene
INVENTOR(S): Luke, Wayne Douglas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005137396	A1	20050623	US 2003-745188	20031222
US 7012153	B2	20060314		
PRIORITY APPLN. INFO.:			US 2003-745188	20031222

OTHER SOURCE(S): CASREACT 143:59836; MARPAT 143:59836
AB The invention relates to a prepn. of benzoic acid derivs. of formula RO2C-p-C6H4-O(CH2)2-3N(R1)R2 [wherein: R is alkyl; R1 and R2 are independently alkyl, or combined together with the nitrogen atom form piperidinyl, pyrrolidinyl, or morpholinyl, etc.], useful as intermediates for preparation of raloxifene. For instance, 4-[2-(piperidin-1- yl)ethoxy]benzoic acid hydrochloride was prepared via etherification of Me 4-hydroxybenzoate by 1-(β-

chloroethyl)piperidine hydrochloride and subsequet hydrolysis with a yield of 99.2%.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:29327 CAPLUS Full-text
DOCUMENT NUMBER: 142:134465
TITLE: Process for preparing raloxifene hydrochloride
INVENTOR(S): Ferrari, Massimo; Zinetti, Fabrizio; Belotti, Paolo
PATENT ASSIGNEE(S): Erregierre S.p.A., Italy
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005003116	A1	20050113	WO 2004-EP51263		20040628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2549354	A1	20050113	CA 2004-2549354		20040628
EP 1641773	A1	20060405	EP 2004-741907		20040628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
US 2007100147	A1	20070503	US 2005-562762		20051227
PRIORITY APPLN. INFO.:			IT 2003-MI1333	A	20030630
			WO 2004-EP51263	W	20040628

OTHER SOURCE(S): CASREACT 142:134465

AB A process for prepg. raloxifene hydrochloride with a purity greater than 98% and low aluminum content comprises the following stages : (a) demethylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene in pyridine and hydrochloric acid to obtain 6-hydroxy-2-(4- hydroxyphenyl)benzo[b]thiophene in pyridine hydrochloride, (b) acetylation of 6-hydroxy-2-(4-hydroxyphonyl)benzo[b]thiophene with an acetylating agent to obtain the corresponding 6-acetoxy-2-(4- acetoxyphenyl)benzo[b]thiophene (I), (c) acylation of 6-acetoxy-2-(4- acetoxyphonyl)benzo[b]thiophene with 4-(2-piperidinoethoxy)benzoylchloride hydrochloride with aluminum trichloride in a halogenated solvent to obtain 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]- benzo[b]thiophene, (d) hydrolysis of 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2- piperidinoethoxy)benzoyl]benzo[b]thiophene according to the following operating conditions: (d1) treatment of 6-acetoxy-2-(4-acetoxyphonyl)-3-[4- (2-piperidinoethoxy)benzoyl]benzo[b]thiophene with alkaline hydroxide in alc. solvent, (d2) acidification of the product obtained in the preceding stage (d1) with a strong acid, to obtain the corresponding raloxifene salt with the strong acid, characterized in that the strong acid used in stage (d2) is concentrated hydrochloric acid. Thus, thionyl chloride was added to a mixture of 4-(2-piperidinoethoxy)benzoic acid HCl salt and pyridine in refluxing methylene chloride; the mixture was stirred for 1 h and

the solvent was distilled off; the mixture was cooled to 20°C, and I was added. The resulting mixture was mixed with aluminum trichloride in methylene chloride at 15°C to 30°C; the mixture was stirred for 1 h and was worked up : the product was treated with sodium hydroxide in methanol; water, Et acetate, and HCl were added; the suspension was centrifuged to give crude raloxifene hydrochloride.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:617920 CAPLUS Full-text
DOCUMENT NUMBER: 142:463529
TITLE: Synthesis of raloxifene hydrochloride
AUTHOR(S): Gong, Ping; Zhao, Yanfang; Wang, Dun
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113
CODEN: SYDXFF; ISSN: 1006-2858
PUBLISHER: Shenyang Yaoke Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 142:463529

AB Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4-hydroxyphenyl)benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3, saponification with 5M NaOH solution in methanol, and saltification with HCl. The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR, 13C NMR.

L6 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:348716 CAPLUS Full-text
DOCUMENT NUMBER: 138:137104
TITLE: Synthesis of Raloxifene hydrochloride as selective estrogen receptor modulator
AUTHOR(S): Chen, Yanzhong; Liu, Yingxiang
CORPORATE SOURCE: Guangdong College of Pharmacy, Canton, 510224, Peop. Rep. China
SOURCE: Guangdong Yaoxueyuan Xuebao (2002), 18(1), 1-3, 20
CODEN: GYXUF8
PUBLISHER: Guangdong Yaoxueyuan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 138:137104

AB Raloxifene was synthesized from α-bromo-p-methoxyacetophenone and m-methoxybenzenethiol via condensation, cyclization, acylation, and demethylation with the overall yield 49.2%. The chemical structure of compound was confirmed by 1H NMR, MS, IR, and elementary anal. The reaction conditions were mild and starting materials were com. available.

L6 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:247325 CAPLUS Full-text
DOCUMENT NUMBER: 134:266100
TITLE: Synthesis of 4-[(2-piperidin-1-yl)ethoxy]benzoic acid for manufacture of Raloxifene hydrochloride

INVENTOR(S): Luke, Wayne Douglas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023369	A2	20010405	WO 2000-US21974	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1220847	A2	20020710	EP 2000-966691	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003510313	T	20030318	JP 2001-526522	20000918

PRIORITY APPLN. INFO.: US 1999-156205P P 19990927
WO 2000-US21974 W 20000918

OTHER SOURCE(S): CASREACT 134:266100; MARPAT 134:266100

AB An improved process for the prepn. of 4[(2-piperidin-1-yl)ethoxy]benzoic acid derivs. comprises reacting haloalkyl amine X(CH2)nNR1R2 (X = halogen; R1, R2 = C1-4 alkyl, combined with nitrogen atom to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, 1-hexamethyleneimino group; n = 2, 3) with C1-6 alkyl p-hydroxybenzoate in the presence of a hydrated inorg. base in an appropriate solvent.

L6 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:12339 CAPLUS Full-text
DOCUMENT NUMBER: 130:66385
TITLE: Process for preparing benzoic acid derivatives as intermediates in the synthesis of benzothiophenes
INVENTOR(S): Chelius, Erik Christopher
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5852193	A	19981222	US 1998-69277	19980429
US 6075146	A	20000613	US 1998-123889	19980728

PRIORITY APPLN. INFO.: US 1997-45162P P 19970430
US 1998-69277 A3 19980429

OTHER SOURCE(S): CASREACT 130:66385; MARPAT 130:66385
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; R6 = carboxy protecting group] were prepared by reacting a hydroxylamine HO(CH2)nNR1R2 with a compound selected from W2O and W-halo (wherein W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.) followed by reaction of the resulting Y1(CH2)nNR1R2 (Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, etc.) with a compound II. Compds. I can be then reacted with benzothiophenes III (R4, R5 = hydroxy protecting groups) to afford compds. IV (R4, R5 = , H, hydroxy protecting groups) (example of such reaction was given).

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:721690 CAPLUS Full-text

DOCUMENT NUMBER: 130:3769

TITLE: Processes for preparing benzothiophenes

INVENTOR(S): McGill, John McNeil, III; Misner, Jerry Wayne; Zhang, Tony Yantao

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9849156	A1	19981105	WO 1998-US8509		19980428
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2287943	A1	19981105	CA 1998-2287943		19980428
AU 9872613	A	19981124	AU 1998-72613		19980428
BR 9809439	A	20000613	BR 1998-9439		19980428
HU 200003187	A2	20010528	HU 2000-3187		19980428
JP 2001522372	T	20011113	JP 1998-547277		19980428
US 6090949	A	20000718	US 1998-69497		19980429
EP 875510	A1	19981104	EP 1998-303374		19980430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
MX 9909883	A	20000331	MX 1999-9883		19991027
PRIORITY APPLN. INFO.:			US 1997-45177P	P	19970430
			WO 1998-US8509	W	19980428

OTHER SOURCE(S): CASREACT 130:3769; MARPAT 130:3769

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y = Cl, Br, I, SO2(C1-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = C1-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:721501 CAPLUS Full-text

DOCUMENT NUMBER: 130:3768

TITLE: Demethylation process for preparing benzo[b]thiophenes

INVENTOR(S): Hoard, David Warren; Luke, Wayne Douglas

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

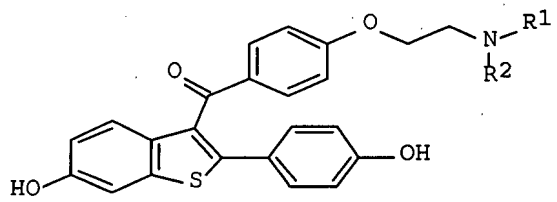
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 875511	A1	19981104	EP 1998-303345		19980429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CA 2236254	A1	19981030	CA 1998-2236254		19980427
JP 11005789	A	19990112	JP 1998-118628		19980428
US 5994547	A	19991130	US 1998-69500		19980429
PRIORITY APPLN. INFO.:			US 1997-45156P	P	19970430

OTHER SOURCE(S): CASREACT 130:3768; MARPAT 130:3768

GI



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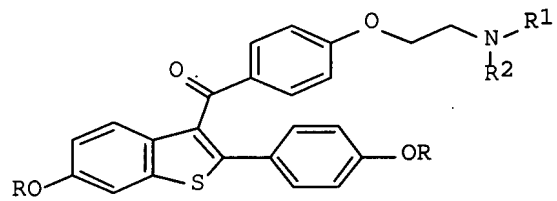


II

AB The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2-methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be

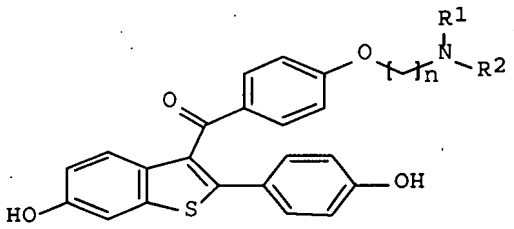
carried out in the same reaction vessel without isolation of the acylated, protected material.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:721498 CAPLUS Full-text
DOCUMENT NUMBER: 130:3767
TITLE: Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceuticals
INVENTOR(S): Chelius, Erik Christopher
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 875507	A1	19981104	EP 1998-303340	19980429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2231013	A1	19981030	CA 1998-2231013	19980304
JP 10316674	A	19981202	JP 1998-116564	19980427

PRIORITY APPLN. INFO.: US 1997-45162P P 19970430
OTHER SOURCE(S): CASREACT 130:3767; MARPAT 130:3767
GI



I

AB The novel intermediates Y1(CH2)nNR1R2 [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, 2,2,2-trifluoroethylsulfonyloxy, trifluoroacetoxy], useful as intermediates in synthesis of benzothiophenes I and their salts, were prepared by reaction a hydroxylamine HO(CH2)nNR1R2 with W2O and W(halo) [W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.].

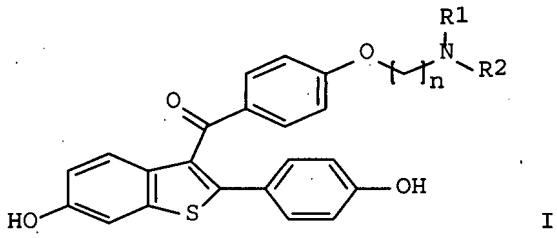
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:719256 CAPLUS Full-text
DOCUMENT NUMBER: 130:3764
TITLE: A regioselective alkylation process for preparing substituted benzo[b]thiophenes
INVENTOR(S): McGill, John McNeil, III; Miller, Randal Scot

PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9848792	A1	19981105	WO 1998-US8477		19980428
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2287918	A1	19981105	CA 1998-2287918		19980428
AU 9871653	A	19981124	AU 1998-71653		19980428
EP 979075	A1	20000216	EP 1998-918798		19980428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI					
JP 2001523252	T	20011120	JP 1998-547259		19980428
US 6025495	A	20000215	US 1998-69276		19980429
PRIORITY APPLN. INFO.:			US 1997-45132P	P	19970430
			WO 1998-US8477	W	19980428

OTHER SOURCE(S): CASREACT 130:3764; MARPAT 130:3764
GI



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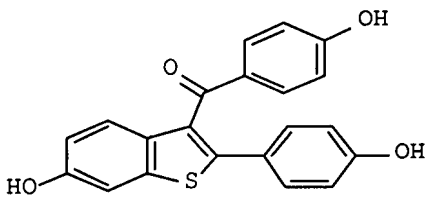


II

AB The title benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2, 3] such as raloxifene, were prepared by the regioselective alkylation of benzothiophene II with Y(CH2)nNR1R2 [Y = Cl, p-TsO] in the presence of a suitable base.

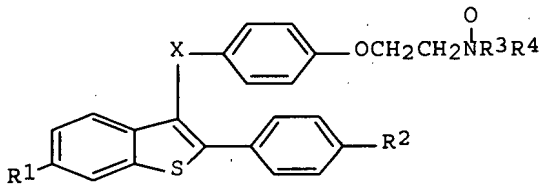
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:192131 CAPLUS Full-text
DOCUMENT NUMBER: 128:275070
TITLE: Benzothiophenes, formulations containing same, and methods
INVENTOR(S): Cullinan, George Joseph; Palkowitz, Alan David
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5731342	A	19980324	US 1997-787041	19970127
PRIORITY APPLN. INFO.:			US 1997-787041	19970127

OTHER SOURCE(S): MARPAT 128:275070
GI



I

AB Benzothiophene N-oxides [I; R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, Cl or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-[2-(1- piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:161136 CAPLUS Full-text
DOCUMENT NUMBER: 128:221639
TITLE: Preparation of amorphous benzothiophenes for pharmaceuticals
INVENTOR(S): Cuff, George W.; Thakkar, Arvind L.

PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Cuff, George W.; Thakkar, Arvind L.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808513	A1	19980305	WO 1997-US14768	19970822
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 826682	A1	19980304	EP 1997-306426	19970822
EP 826682	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2263175	A1	19980305	CA 1997-2263175	19970822
AU 9742335	A	19980319	AU 1997-42335	19970822
AU 723987	B2	20000907		
IN 182940	A1	19990814	IN 1997-CA1549	19970822
BR 9713176	A	20000208	BR 1997-13176	19970822
CN 1244124	A	20000209	CN 1997-197434	19970822
HU 200001172	A2	20010628	HU 2000-1172	19970822
HU 200001172	A3	20020128		
NZ 333839	A	20010629	NZ 1997-333839	19970822
IL 128641	A	20011031	IL 1997-128641	19970822
TR 9900403	T2	20020121	TR 1999-403	19970822
JP 2002514174	T	20020514	JP 1998-511744	19970822
AT 234295	T	20030315	AT 1997-306426	19970822
ES 2195089	T3	20031201	ES 1997-306426	19970822
ZA 9707617	A	19990225	ZA 1997-7617	19970825
US 6713494	B1	20040330	US 1997-918741	19970825
NO 9900914	A	19990225	NO 1999-914	19990225
KR 2000035941	A	20000626	KR 1999-701682	19990227

PRIORITY APPLN. INFO.: US 1996-24831P P 19960828
WO 1997-US14768 W 19970822

OTHER SOURCE(S): MARPAT 128:221639

AB A method for prepg. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:640660 CAPLUS Full-text
DOCUMENT NUMBER: 127:307297
TITLE: Preparation of 3-[4-(2-aminoethoxy)benzoyl]-2-aryl-6-hydroxybenzo[b]thiophenes.
INVENTOR(S): Jones, Charles David; McGill, John McNeill, III
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Jones, Charles David; McGill,

	John McNeill, III
SOURCE:	PCT Int. Appl., 33 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9734888	A1	19970925	WO 1996-US3934		19960320
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2249406	A1	19970925	CA 1996-2249406		19960320
AU 9652586	A	19971010	AU 1996-52586		19960320
EP 888331	A1	19990107	EP 1996-908892		19960320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 2000506885	T	20000606	JP 1997-533424		19960320
US 6008377	A	19991228	US 1998-125848		19980821
PRIORITY APPLN. INFO.:			US 1996-13674P	P	19960319
			WO 1996-US3934	W	19960320

OTHER SOURCE(S): CASREACT 127:307297; MARPAT 127:307297

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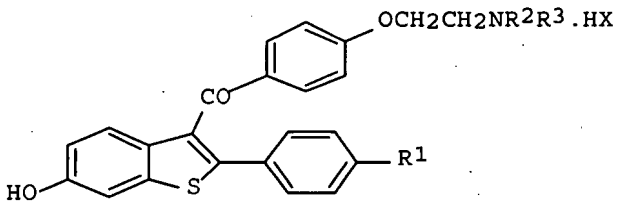

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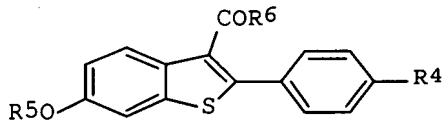

II

AB Title compds. (I; R1 = H, OH; R2, R3 = alkyl; R2R3N = pyrrolidino, piperidino, hexamethyleneimino, morpholino; HX = HCl, HBr) were prepared by reaction of PhOCH2CH2NR2R3.HX (variables as above) with acyl derivative (II; R4 = H, alkoxy; R5 = alkyl; R6 = Cl, Br, OH) in the presence of BX3. Thus, 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene-3-carbonyl chloride (preparation given), and Ph 2-N-piperidinylethyl ether hydrochloride (preparation given) in 1,2-dichloroethane at 0° were treated with BCl3 in 1,2-dichloroethane at 0° followed by warming to 35° for 16-20 h to give 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2- piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride 1,2-dichloroethane solvate.

L6 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:124441 CAPLUS Full-text
DOCUMENT NUMBER: 126:143973
TITLE: Diaryl vinyl sulfoxides, a process for their synthesis, and their use in the preparation of benzothiophene derivatives
INVENTOR(S): Aikins, James A.; Miller, Randal S.; Zhang, Tony Y.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Aikins, James A.; Miller, Randal S.; Zhang, Tony Y.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640691	A1	19961219	WO 1996-US9163	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
US 5659087	A	19970819	US 1995-478706	19950607
US 6372945	B1	20020416	US 1995-483130	19950607
CA 2220145	A1	19961219	CA 1996-2220145	19960604
AU 9660920	A	19961230	AU 1996-60920	19960604
AU 697352	B2	19981001		
EP 830361	A1	19980325	EP 1996-918211	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192741	A	19980909	CN 1996-196167	19960604
BR 9608579	A	19990105	BR 1996-8579	19960604
JP 11507061	T	19990622	JP 1996-501552	19960604
HU 9900922	A2	19990728	HU 1999-922	19960604
HU 9900922	A3	20000628		
NZ 337030	A	20001124	NZ 1996-337030	19960604
NZ 337031	A	20010126	NZ 1996-337031	19960604
SG 106558	A1	20041029	SG 1998-4999	19960604
NO 9705578	A	19971203	NO 1997-5578	19971203
NO 5987	A	19971203	NO 2000-5987	20001127
CN 1341596	A	20020327	CN 2000-130779	20001215

PRIORITY APPLN. INFO.:		
US 1995-478706	A	19950607
US 1995-483130	A	19950607
NZ 1996-310179	A1	19960604
WO 1996-US9163	W	19960604

OTHER SOURCE(S): CASREACT 126:143973; MARPAT 126:143973
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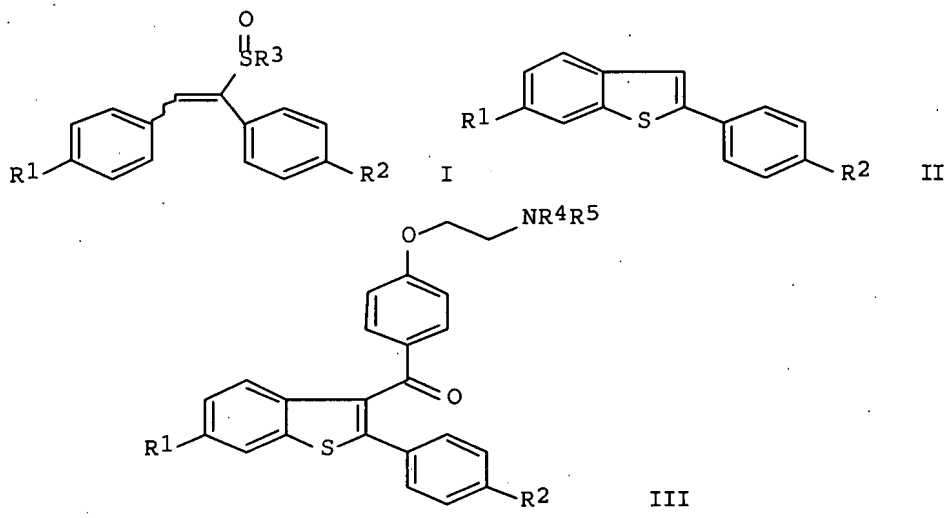


AB The invention is directed to new diarylvinyl sulfoxides I [R1, R2 = H, alkoxy, arylalkoxy, halo, amino; R3 = thermally labile or acid-labile alkyl, alkenyl, or arylalkyl group], and to a new process for their synthesis. I are useful precursors for 2-aryl-substituted benzothiophenes II, which are in turn intermediates for the drugs III.HX [R1, R2 = H, halo, amino, OH; R4, R5 = alkyl; or NR4R5 = pyrrolidino, piperidino, hexamethyleneimino, morpholino; X = Cl, Br]. For instance, treatment of 4-MeOC6H4CH2COC6H4OMe-4 with TiCl4 in THF and reaction with Me3CSH and Et3N gave the vinyl sulfide (E)-4-MeOC6H4CH:C(SCMe3)C6H4OMe-4 [(E)-IV]. Alternatively, lithiation of 4-MeOC6H4CH2SCMe3 with BuLi and condensation with 4-MeOC6H4CHO gave (Z)-IV. Oxidation of either isomer of IV with a dilute AcOH solution of peracetic acid, in PhMe at -20°, gave the corresponding sulfoxide I [R1 = R2 = OMe; R3 = CMe3]. Dehydrative cyclization of, e.g., the (E)-sulfoxide, using p-MeC6H4SO3H catalyst under Dean-Stark conditions in PhMe, gave the benzothiophene II [R1 = R2 = OMe]. This was acylated by 4-(2-piperidinoethoxy)benzoyl chloride HCl in the presence of BCl3 with concomitant demethylation to give the objective compound III.HCl [R1 = R2 = OH, NR4R5 = piperidino].

L6 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:113406 CAPLUS Full-text
DOCUMENT NUMBER: 126:117861
TITLE: Process for the synthesis of benzo(b)thiophenes
INVENTOR(S): Aikins, James A.; Zhang, Tony Y.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Aikins, James A.; Zhang, Tony Y.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640676	A1	19961219	WO 1996-US9167	19960604

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,

LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

US 5606076	A	19970225	US 1995-484536	19950607
CA 2223096	A1	19961219	CA 1996-2223096	19960604
AU 9660921	A	19961230	AU 1996-60921	19960604
AU 702928	B2	19990311		
EP 859770	A1	19980826	EP 1996-918212	19960604
EP 859770	B1	19991208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192211	A	19980902	CN 1996-195943	19960604
CN 1086699	B	20020626		
BR 9609062	A	19990126	BR 1996-9062	19960604
JP 11506789	T	19990615	JP 1997-501555	19960604
HU 9900912	A2	19990728	HU 1999-912	19960604
HU 9900912	A3	20000328		
HU 219735	B	20010730		
AT 187450	T	19991215	AT 1996-918212	19960604
ES 2140859	T3	20000301	ES 1996-918212	19960604
PT 859770	T	20000531	PT 1996-918212	19960604
IL 131440	A	20001031	IL 1996-131440	19960604
IL 122378	A	20010319	IL 1996-122378	19960604
NO 9705582	A	19971203	NO 1997-5582	19971203
GR 3032666	T3	20000630	GR 2000-400364	20000214

PRIORITY APPLN. INFO.:	US 1995-484536	A	19950607
	IL 1996-122378	A3	19960604
	WO 1996-US9167	W	19960604

OTHER SOURCE(S): CASREACT 126:117861; MARPAT 126:117861

AB The present invention is directed to a process for the synthesis of 2-arylbenzo[b]thiophenes. E.g., 6-methoxy-2-(4- methoxyphenyl)benzo[b]thiophene was prepared from desoxyanisoin and 2-methyl-2-propanethiol via tert-Bu 4,4'-dimethoxystilbenyl sulfoxide.

L6 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

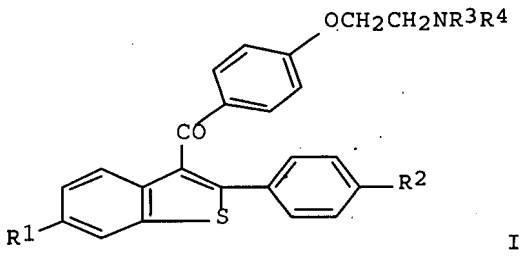
ACCESSION NUMBER:	1996:649600 CAPLUS Full-text
DOCUMENT NUMBER:	125:266032
TITLE:	Phosphorous-containing benzothiophenes, their preparation, their use in treating postmenopausal syndrome-associated indications and estrogen-dependent diseases, and pharmaceuticals containing them
INVENTOR(S):	Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey S.
PATENT ASSIGNEE(S):	Eli Lilly and Co., USA
SOURCE:	Eur. Pat. Appl., 19 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 729964	A1	19960904	EP 1996-300878	19960209
EP 729964	B1	20010509		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 6479517	B1	20021112	US 1995-395944	19950228
ES 2158242	T3	20010901	ES 1996-300878	19960209

CA 2169414	A1	19960829	CA 1996-2169414		19960213
JP 08259560	A	19961008	JP 1996-25281		19960213
US 5998443	A	19991207	US 1997-946842		19971008
PRIORITY APPLN. INFO.:			US 1995-395944	A	19950228

OTHER SOURCE(S): MARPAT 125:266032

GI



I

AB Phosphorus-contg. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(O-alkyl)2, OPO(O-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3-dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds. of the invention, as well as pharmaceutical compns. containing compds. of the invention.

L6 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:319150 CAPLUS Full-text

DOCUMENT NUMBER: 125:86484

TITLE: Preparation of vinyl sulfenic acid derivatives as benzo[b]thiophene intermediates

INVENTOR(S): Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 15 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5512701	A	19960430	US 1995-482692	19950607
CA 2224225	A1	19961219	CA 1996-2224225	19960604
WO 9640693	A1	19961219	WO 1996-US9460	19960604

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,

SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM

AU 9661003	A	19961230	AU 1996-61003		19960604
AU 698076	B2	19981022			
EP 830362	A1	19980325	EP 1996-918314		19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
CN 1192215	A	19980902	CN 1996-195947		19960604
CN 1068883	B	20010725			
BR 9608847	A	19990608	BR 1996-8847		19960604
JP 11507346	T	19990629	JP 1997-501774		19960604
HU 9900923	A2	19990728	HU 1999-923		19960604
HU 9900923	A3	20000228			
IL 122127	A	20010520	IL 1996-122127		19960604
NO 9705633	A	19980128	NO 1997-5633		19971204
CN 1330071	A	20020109	CN 2000-130796		20001212
PRIORITY APPLN. INFO.:			US 1995-482692	A	19950607
			US 1995-483607	A	19950607
			WO 1996-US9460	W	19960604

OTHER SOURCE(S): CASREACT 125:86484; MARPAT 125:86484

AB 4-R1C6H4CH:C(R9)C6H4R2-4 [I; R1,R2 = H, (ar)alkoxy, halo, NH2; R9 = SR4; R4 = OSi(R)3, NR5R6, SR8; R = (ar)alkyl, aryl; R5,R6 = H, (ar)alkyl; NR5R6 = pyrrolidino, piperidino, etc.; R8 = (ar)alkyl, aryl] were prepared by treating I [R9 = SOR3; R3 = labile alk(en)yl or aryl] with a silylating agent optionally followed by reaction with HNR5R6 or HSR8. Thus, (E)-I (R1 = R2 = OMe)(II; R9 = SOCMe3)(preparation given) was treated with (Me2CSiNH)2CO in PhMe followed by Me2NH, in the same pot, to give I (R1 = R2 = OMe, R9 = SNMe2) as a mixture of (E)- and (Z)-isomers. The latter mixt was treated with TsOH to give 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophe ne.

L6 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:307324 CAPLUS Full-text
DOCUMENT NUMBER: 124:343103
TITLE: Preparation of unsolvated crystalline 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride.
INVENTOR(S): Smith Labell, Elizabeth; Luke, Wayne Douglas; McNeill McGill, John, III; Miller, Randal Scot
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19534744	A1	19960321	DE 1995-19534744	19950919
US 5629425	A	19970513	US 1994-308325	19940919
IN 1995CA00614	A	20050304	IN 1995-CA614	19950530
IN 1995CA00615	A	20050304	IN 1995-CA615	19950530
TW 389760	B	20000511	TW 1995-84105614	19950605
TW 412534	B	20001121	TW 1995-84105613	19950605
US 5731327	A	19980324	US 1995-467485	19950606
EG 21479	A	20011128	EG 1995-455	19950606
US 6399778	B1	20020604	US 1995-469093	19950606

US 6472531	B1	20021029	US 1995-469961	19950606
ES 2109882	A1	19980116	ES 1995-1774	19950913
ES 2109882	B1	19980816		
ES 2129293	A1	19990601	ES 1995-1775	19950913
ES 2129293	B1	20000116		
NL 1001194	A1	19960319	NL 1995-1001194	19950914
NL 1001194	C2	19970404		
NL 1001196	A1	19960319	NL 1995-1001196	19950914
NL 1001196	C2	19970404		
ZA 9507752	A	19970314	ZA 1995-7752	19950914
ZA 9507753	A	19970314	ZA 1995-7753	19950914
IL 115315	A	19990922	IL 1995-115315	19950914
IL 115314	A	20000229	IL 1995-115314	19950914
IL 125283	A	20010614	IL 1995-125283	19950914
IN 1995CA01111	A	20051021	IN 1995-CA1111	19950914
CA 2158399	A1	19960320	CA 1995-2158399	19950915
CA 2158399	C	20010320		
CA 2158400	A1	19960320	CA 1995-2158400	19950915
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DK 9501027	A	19960320	DK 1995-1027	19950915
DK 175903	B1	20050606		
DK 9501028	A	19960320	DK 1995-1028	19950915
DK 175897	B1	20050530		
NO 9503657	A	19960320	NO 1995-3657	19950915
NO 308107	B1	20000724		
NO 9503658	A	19960320	NO 1995-3658	19950915
NO 313996	B1	20030113		
SE 9503213	A	19960320	SE 1995-3213	19950915
SE 520721	C2	20030812		
SE 9503214	A	19960320	SE 1995-3214	19950915
SE 509265	C2	19981221		
RO 115259	B1	19991230	RO 1995-1619	19950915
RO 115260	B1	19991230	RO 1995-1620	19950915
CZ 290343	B6	20020717	CZ 1995-2403	19950915
CZ 292007	B6	20030716	CZ 1995-2402	19950915
FI 9504402	A	19960320	FI 1995-4402	19950918
FI 112226	B1	20031114		
FI 9504403	A	19960320	FI 1995-4403	19950918
FR 2724655	A1	19960322	FR 1995-10921	19950918
FR 2724655	B1	19971114		
GB 2293382	A	19960327	GB 1995-19028	19950918
GB 2293382	B	19980819		
GB 2293602	A	19960403	GB 1995-19032	19950918
GB 2293602	B	19980506		
AU 9531730	A	19960404	AU 1995-31730	19950918
AU 691955	B2	19980528		
AU 9531731	A	19960404	AU 1995-31731	19950918
AU 692907	B2	19980618		
JP 08176147	A	19960709	JP 1995-238211	19950918
JP 2860071	B2	19990224		
CN 1127253	A	19960724	CN 1995-118629	19950918
CN 1075069	B	20011121		
JP 08193081	A	19960730	JP 1995-238209	19950918
LV 11177	B	19960820	LV 1995-284	19950918
LV 11178	B	19960820	LV 1995-285	19950918
BR 9504059	A	19960924	BR 1995-4059	19950918
BR 9504060	A	19960924	BR 1995-4060	19950918
FR 2732020	A1	19960927	FR 1995-10922	19950918
FR 2732020	B1	19971114		
CN 1132205	A	19961002	CN 1995-118449	19950918

CN 1068324	B	20010711			
HU 74178	A2	19961128	HU 1995-2723		19950918
HU 75033	A2	19970328	HU 1995-2721		19950918
HU 225417	B1	20061128			
BE 1009625	A3	19970603	BE 1995-760		19950918
BE 1009626	A3	19970603	BE 1995-761		19950918
RU 2104278	C1	19980210	RU 1995-116242		19950918
RU 2108331	C1	19980410	RU 1995-116238		19950918
AT 9501542	A	20001215	AT 1995-1542		19950918
CH 691125	A5	20010430	CH 1995-2629		19950918
CH 691431	A5	20010731	CH 2000-2062		19950918
CH 691478	A5	20010731	CH 1995-2628		19950918
CH 691594	A5	20010831	CH 1995-1780		19950918
PL 182450	B1	20020131	PL 1995-310518		19950918
HR 950483	B1	20030228	HR 1995-483		19950918
PL 187686	B1	20040930	PL 1995-310517		19950918
HR 950482	B1	20070430	HR 1995-482		19950918
AT 502957	A1	20070615	AT 1995-1543		19950918
WO 9609045	A1	19960328	WO 1995-US11872		19950919
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
DE 19534745	A1	19960404	DE 1995-19534745		19950919
DE 19534745	B4	20040609			
AU 9537186	A	19960409	AU 1995-37186		19950919
EE 3386	B1	20010416	EE 1997-55		19950919
SK 283502	B6	20030805	SK 1997-233		19950919
DE 19549755	B4	20050504	DE 1995-19549755		19950919
DK 9700027	A	19970109	DK 1997-27		19970109
DK 175887	B1	20050523			
DK 9700028	A	19970109	DK 1997-28		19970109
DK 175886	B1	20050523			
CZ 290344	B6	20020717	CZ 2001-3548		20011002
US 2002173645	A1	20021121	US 2002-83179		20020226
PRIORITY APPLN. INFO.:			US 1994-308325	A	19940919
			US 1995-427914	A	19950426
			US 1995-469093	A1	19950606
			IL 1995-115315	A3	19950914
			CZ 1995-2402	A3	19950915
			DE 1995-19534744	A1	19950919
			WO 1995-US11872	W	19950919

AB Title compd. (I) (raloxifene hydrochloride) having a specified X-ray diffraction pattern, was prepared Thus, 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene (preparation given) and 4-(2-piperidinoethoxy)benzoyl chloride hydrochloride (preparation given) in CH2Cl2 was treated with BCl3 at 0 for 8 h and at 35° for 16 h to give I.1,2-dichloroethane of 86.8% purity. The latter in MeOH was treated with NaOH and activated C followed by filtration, treatment with HCl, and crystallization to give 99.1% pure I.

L6 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:256453 CAPLUS Full-text
DOCUMENT NUMBER: 124:289251
TITLE: Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceutical agents

INVENTOR(S): Kjell, Douglas Patton; Perry, Fred Mason
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 699672	A1	19960306	EP 1995-306050	19950830
EP 699672	B1	19980422		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5631369	A	19970520	US 1994-298636	19940831
IL 128881	A	20001206	IL 1995-128881	19950828
CA 2157236	A1	19960301	CA 1995-2157236	19950830
FI 9504067	A	19960301	FI 1995-4067	19950830
HU 73141	A2	19960628	HU 1995-2537	19950830
HU 222121	B1	20030428		
BR 9503846	A	19960917	BR 1995-3846	19950830
AT 165355	T	19980515	AT 1995-306050	19950830
ES 2114721	T3	19980601	ES 1995-306050	19950830
TW 427975	B	20010401	TW 1995-84109069	19950830
JP 08119964	A	19960514	JP 1995-223183	19950831
US 5750688	A	19980512	US 1996-629862	19960409

PRIORITY APPLN. INFO.: US 1994-298636 A 19940831
IL 1995-115092 A3 19950828

OTHER SOURCE(S): MARPAT 124:289251
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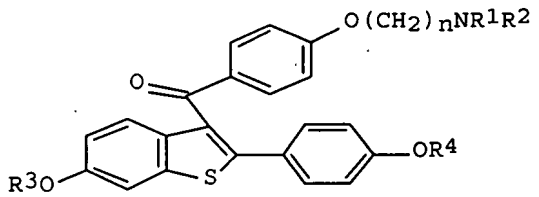

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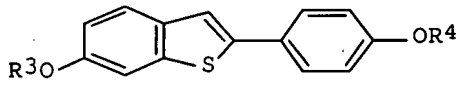

II

AB The present invention provides a novel process for prepg. novel compds. of formula HO2C(p-C6H4)O(CH2)nNR1R2 [R1, R2 = C1-C4 alkyl, combine to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2)nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compds. of formula RO2C(p-C6H4)OH [R = C1-C6 alkyl], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product of step (a) with an aqueous acid; and (c) cleaving the ester of the reaction product from step (b) to form an acid. The present invention further provides a novel process for preparing compds. of Formula I [R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidino, methylpyrrolidino, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1-

hexamethyleneimino; R3, R4 = H, hydroxy protecting group; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2)nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compound of formula RO2C(p-C6H4)OH [R = C1-C6 alky], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product from step (a) with an aqueous acid; (c) cleaving the ester of the reaction product from step (b) to form an acid; (d) reacting the extracted product from step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing R3 and R4 hydroxy protecting groups of the reaction product from step (d); and (f) optionally forming a salt of the reaction from either steps (d) or step (e).

L6 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:150242 CAPLUS Full-text
DOCUMENT NUMBER: 124:202950
TITLE: Preparation of benzothiophene glucopyranosides as antihyperlipidemics.
INVENTOR(S): Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom, Terry Donald; Lugar, Charles Willis Iii; Staten, Gilbert Stanley
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 683170	A1	19951122	EP 1995-303265	19950516
EP 683170	B1	19990922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5567820	A	19961022	US 1995-404701	19950315
US 6723739	B1	20040420	US 1995-405555	19950315
CA 2149501	A1	19951121	CA 1995-2149501	19950516
ZA 9503975	A	19961118	ZA 1995-3975	19950516
AT 184880	T	19991015	AT 1995-303265	19950516
ES 2136799	T3	19991201	ES 1995-303265	19950516
AU 9520121	A	19951130	AU 1995-20121	19950517
AU 683734	B2	19971120		
JP 07316180	A	19951205	JP 1995-118338	19950517
FI 9502420	A	19951121	FI 1995-2420	19950518
NO 9501954	A	19951121	NO 1995-1954	19950518
NO 304686	B1	19990201		
CN 1116626	A	19960214	CN 1995-106322	19950518
CN 1039013	B	19980708		
BR 9502079	A	19960305	BR 1995-2079	19950518
HU 73788	A2	19960930	HU 1995-1466	19950518
HU 219335	B	20010328		
IL 113780	A	19990620	IL 1995-113780	19950518
GR 3032142	T3	20000427	GR 1999-403228	19991215
US 2004167080	A1	20040826	US 2004-778865	20040212
PRIORITY APPLN. INFO.:			US 1994-246655 A	19940520
			US 1995-405555 A1	19950315

OTHER SOURCE(S): CASREACT 124:202950
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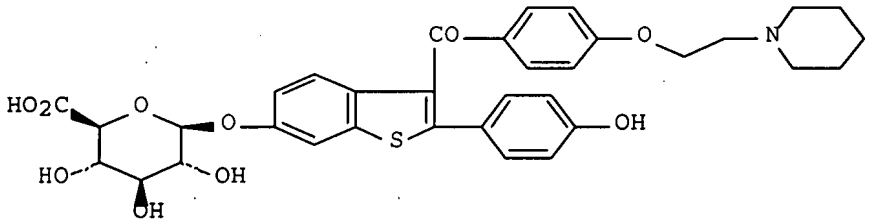

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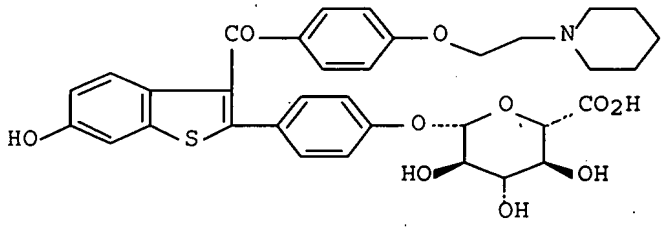

II

AB Raloxifene metabolites (I) and (II) and their hydrochloride salts were prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-O-tetraacetyl-D-glucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

L6 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:123714 CAPLUS Full-text
DOCUMENT NUMBER: 124:155994
TITLE: Pharmaceutical compositions containing 2-phenyl-3-aryoylbenzothiophenes for for inhibiting bone loss and lowering serum cholesterol
INVENTOR(S): Draper, Michael W.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Can. Pat. Appl., 31 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2141999	A1	19950903	CA 1995-2141999	19950207
US 5478847	A	19951226	US 1994-205012	19940302
ZA 9500976	A	19960807	ZA 1995-976	19950207
NZ 314699	A	20000728	NZ 1995-314699	19950207
EP 674903	A1	19951004	EP 1995-300842	19950210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9500774	A	19950904	NO 1995-774	19950228
RU 2100024	C1	19971227	RU 1995-102778	19950228
RU 2150275	C1	20000610	RU 1996-119781	19950228
AU 9513551	A	19950907	AU 1995-13551	19950301
AU 702575	B2	19990225		
JP 07267861	A	19951017	JP 1995-41769	19950301
JP 2818384	B2	19981030		

BR 9500784	A	19951024	BR 1995-784		19950301
CN 1119530	A	19960403	CN 1995-100021		19950301
HU 72638	A2	19960528	HU 1995-634		19950301
JP 10291932	A	19981104	JP 1998-107550		19950301
JP 10310525	A	19981124	JP 1998-107549		19950301
US 5610168	A	19970311	US 1995-422289		19950414
US 5641790	A	19970624	US 1995-422417		19950414
US 5747510	A	19980505	US 1997-788984		19970127
US 39050	E1	20060328	US 2003-375274		20030227
PRIORITY APPLN. INFO.:			US 1994-205012	A	19940302
			JP 1995-41769	A3	19950301
			US 1995-422417	A1	19950414

AB A method of inhibiting bone loss or resorption, or lowering serum cholesterol, comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in post-menopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

L6 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:991025 CAPLUS Full-text
DOCUMENT NUMBER: 124:106673
TITLE: Methods for lowering serum cholesterol
INVENTOR(S): Black, Larry J.; Bryant, Henry U.; Cullinan, George J.; Kauffman, Raymond F.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5464845	A	19951107	US 1993-159159	19931130
TW 383306	B	20000301	TW 1993-82100751	19930204
RU 2123335	C1	19981220	RU 1993-55026	19931213
ZA 9309427	A	19950615	ZA 1993-9427	19931215
SK 279271	B6	19980805	SK 1993-1421	19931215
IL 108042	A	19980104	IL 1993-108042	19931216
CZ 283863	B6	19980617	CZ 1993-2790	19931216
HU 69686	A2	19950928	HU 1993-3676	19931220
HU 223342	B1	20040628		
RO 113806	B1	19981130	RO 1993-1739	19931220
PL 177349	B1	19991029	PL 1993-301579	19931220
CA 2112017	A1	19940623	CA 1993-2112017	19931221
CA 2112017	C	20050614		
NO 9304740	A	19940623	NO 1993-4740	19931221
AU 9352578	A	19940707	AU 1993-52578	19931221
AU 669235	B2	19960530		
BR 9305182	A	19940816	BR 1993-5182	19931221
JP 06234632	A	19940823	JP 1993-323825	19931222
JP 3197129	B2	20010813		
CN 1094042	A	19941026	CN 1993-121277	19931222
CN 1043608	B	19990616		
AT 233559	T	20030315	AT 1993-310438	19931222

ES 2193142	T3	20031101	ES 1993-310438	19931222
PRIORITY APPLN. INFO.:			US 1992-995222	B2 19921222
OTHER SOURCE(S):	MARPAT 124:106673			

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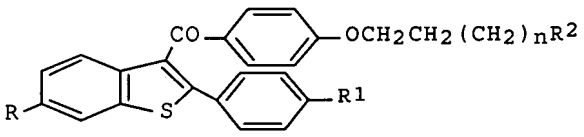

I

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof. The tested compds. lowered LDL without significantly affecting primary sex targets.

L6 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1995:934099 CAPLUS Full-text
DOCUMENT NUMBER:	123:339764
TITLE:	Processes for preparing 3-(benzoyl)-2-(4-hydroxyphenyl)benzothiophenes
INVENTOR(S):	Dodge, Jeffrey Alan; Stocksdale, Mark Gregory
PATENT ASSIGNEE(S):	Eli Lilly and Co., USA
SOURCE:	Eur. Pat. Appl., 19 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 675121	A1	19951004	EP 1995-302076	19950328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2145614	A1	19951001	CA 1995-2145614	19950327
JP 07278138	A	19951024	JP 1995-73418	19950330
US 5808061	A	19980915	US 1995-503444	19950717

PRIORITY APPLN. INFO.:		US 1994-220853	A 19940331
OTHER SOURCE(S):	CASREACT 123:339764; MARPAT 123:339764		

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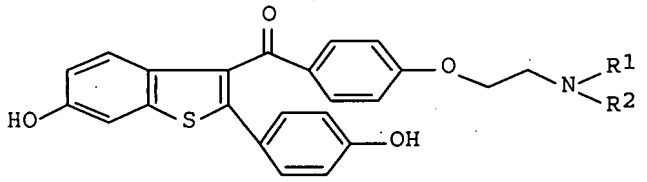

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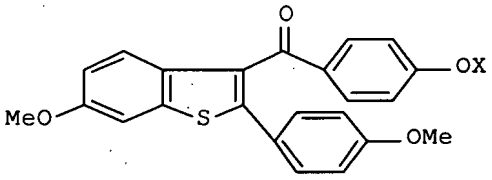

II

AB The title compds. [I; R1R2 = C4-6 polymethylene, CH2CH(CH3)CH2CH2, CH2C(CH3)2CH2CH2, CH2CH2OCH2CH2] [e.g., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride], useful for the treatment of osteoporosis in post-menopausal women (no data), are prepared by: (a) coupling a benzothiophene (II; X = H) with a (hydroxyethyl)amine HOCH2CH2N(R1)R2 in the presence of P(Ph3) and di-Et azodicarboxylate; or (b) reacting a benzothiophene (II; X = CH2CH2Z; Z = leaving group) with pyrrolidine, piperidine, hexamethyleneimine, methylpyrrolidine, dimethylpyrrolidine, or morpholine; (c) deprotecting the 6- and 4-position hydroxy groups of the reaction product of step (a) or step (b); and (d) optionally salifying or forming a solvate of the reaction product of step (c).

L6 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:661193 CAPLUS Full-text
DOCUMENT NUMBER: 123:111843
TITLE: 2-amino-3-aroylbenzo[b]thiophenes and methods for preparing and using same to produce 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-aminoethoxy)benzoyl]benzo[b]thiophene
INVENTOR(S): Godfrey, Alexander G.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5420349	A	19950530	US 1994-258641	19940610
CA 2192096	A1	19951221	CA 1995-2192096	19950607
WO 9534536	A1	19951221	WO 1995-US7399	19950607
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9528236	A	19960105	AU 1995-28236	19950607

EP 764150	A1	19970326	EP 1995-923804		19950607
EP 764150	B1	19991027			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
HU 76000	A2	19970630	HU 1996-3404		19950607
HU 213834	B	19971028			
HU 76525	A2	19970929	HU 1996-3403		19950607
HU 216272	B	19990528			
BR 9507968	A	19971118	BR 1995-7968		19950607
JP 10503175	T	19980324	JP 1996-502366		19950607
AT 186050	T	19991115	AT 1995-923804		19950607
ES 2139222	T3	20000201	ES 1995-923804		19950607
HU 217822	B	20000428	HU 1998-2648		19950607
FI 9604854	A	19961204	FI 1996-4854		19961204
GR 3032409	T3	20000531	GR 2000-400106		20000119
PRIORITY APPLN. INFO.:			US 1994-258641	A	19940610
			WO 1995-US7399	W	19950607

OTHER SOURCE(S): CASREACT 123:111843; MARPAT 123:111843

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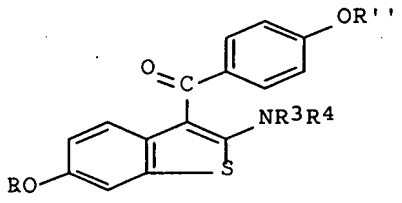

I

AB A group of 2-amino-3-aroyl-benzo[b]thiophenes (I) are prepd. by prepg. an α-hydroxy thioacetamide 4-ROC6H4CH(OH)C(:S)NR9R9 (II) wherein R, R8 and R9 independently represent C1-C6 alkyl; comprising: (a) reacting an alkyl imidate of the formula 4-ROC6H4CH(OH)C(:NH.protic acid)OR''' where R''' is C1-C6 alkyl, with a sulfur compound to yield a thioester of the formula 4-ROC6H4CH(OH)C(:S)OR'''; (b) reacting the thioester with a dialkylamine of the formula HNR8R9 to yield the α-hydroxy thioacetamide; said steps being conducted without isolation or purification of the thioester., cyclizing II, and subsequently acylating the benzo[b]thiophene to yield the 2-amino-3-aryl derivative These compds. may be treated with suitable Ph Grignard reagents, and after deprotection, yield 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thi ophene. %Thus, e.g., p-anisaldehyde was converted to p- methoxybenzaldehyde cyanohydrin (80% yield) and subsequently to the Me imidate 4-MeOC6H4CH(OH)C(:NH.HCl)OMe (85-90% yield); reaction of the latter with H2S/Me2NH afforded α-(4-methoxy phenyl)-α-hydroxy- N,N-dimethylthioacetamide (70%) which was cyclized with methanesulfonic acid to 2-N,N-dimethylamino-6-methoxybenzo[b]thiophene (79%); acylation of the latter with 4-(2-piperidinoethoxy)benzoyl chloride hydrochloride (autocatalytic) afforded 2-N,N-dimethylamino-6-methoxy-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (I; R = Me, R3 = R4 = Me, R'' = 2-piperidinoethyl; 74%) which underwent Grignard reaction with 4-methoxyphenylmagnesium bromide to afford 2-(4-methoxyphenyl)-6- methoxy-3-[4-(piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (90%); deprotection of the latter with AlCl3/propanethiol afforded 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thi ophene hydrochloride (95% yield).

ACCESSION NUMBER: 1995:362913 CAPLUS Full-text
DOCUMENT NUMBER: 122:213884
TITLE: A chemical probe for the estrogen receptor: synthesis of the 3H-isotopomer of raloxifene
AUTHOR(S): Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C. David
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (1995), 36(1), 43-9
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate was accessed by regioselective aroylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1-piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me ethers in the presence of the ethoxy side-chain followed by palladium catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

L6 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:433189 CAPLUS Full-text
DOCUMENT NUMBER: 107:33189
TITLE: Treatment of mammary cancer
INVENTOR(S): Black, Larry J.; Clemens, James A.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 10 pp. Cont. of U.S. Ser. No. 289,360, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4656187	A	19870407	US 1983-556875	19831201
PRIORITY APPLN. INFO.:			US 1981-289360	A1 19810803

AB A method of inhibiting the growth of estrogen-dependent mammary cancers comprises administering about 20 mg/kg/day of a 1st compound 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-pyrrolidinoethoxy)benzoyl]benzo[b]th iophene (I) and .apprx.5 mg/kg/day of a 2nd compound tamoxifen (II). Also, a pharmaceutical combination comprises .apprx.4 parts by weight of I and .apprx.1 part by weight of II. I hydrochloride was prepared by reacting 4-(2-pyrrolidinoethoxy)benzoic acid with thionyl chloride and then with 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene (prepared from 3-methoxybenzenethiol and α-bromo-4-methoxyacetophenone). Oral doses of I 20 and II 5 mg/kg/day were given for 8 wks to rats with induced mammary tumors. Half of the rats receiving the combination treatment experienced a total regression of their tumors. The rest had only a very modest growth of their tumors during the treatment. A synergistic effect was shown.

L6 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:448784 CAPLUS Full-text
DOCUMENT NUMBER: 101:48784

TITLE: Antiestrogens. 2. Structure-activity studies in a series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone hydrochloride (LY 156758), a remarkably effective estrogen antagonist with only minimal intrinsic estrogenicity

AUTHOR(S): Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.; Peters, Mary K.; Black, Larry J.; Thompson, Allen R.; Falcone, Julie F.; Clemens, James A.

CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA

SOURCE: Journal of Medicinal Chemistry (1984), 27(8), 1057-66
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

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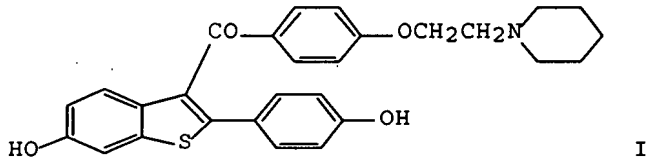


I

AB In an effort to prep. nonsteroidal antiestrogens demonstrating greater antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b]thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino)ethoxy side chain functionality elsewhere in the mol. was AlCl3/EtSH. The benzothiophene derivs. were tested for their ability to inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1- piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. In antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

L6 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:156501 CAPLUS Full-text

DOCUMENT NUMBER: 100:156501

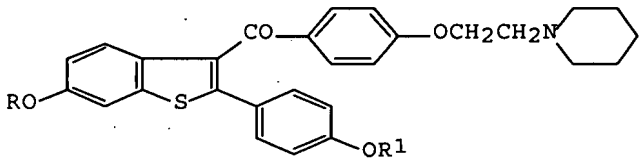
TITLE: Antiestrogenic and antiandrogenic benzothiophenes

INVENTOR(S): Jones, Charles D.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4418068	A	19831129	US 1981-331042	19811216
ZA 8202247	A	19831130	ZA 1982-2247	19820401

PRIORITY APPLN. INFO.: US 1981-246335 A2 19810403
OTHER SOURCE(S): CASREACT 100:156501
GI



I

AB Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un)substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2-piperidinoethoxy)benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered 0.03 μg estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

L6 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:422309 CAPLUS Full-text
DOCUMENT NUMBER: 99:22309
TITLE: Acylated benzothiophenes
INVENTOR(S): Peters, Mary K.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 246,333, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4380635	A	19830419	US 1981-331046	19811216
CA 1167036	A1	19840508	CA 1982-400262	19820331
EP 62505	A1	19821013	EP 1982-301739	19820401

EP 62505	B1	19850724			
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
GB 2096608	A	19821020	GB 1982-9681		19820401
GB 2096608	B	19850612			
DD 201794	A5	19830810	DD 1982-238653		19820401
CS 227347	B2	19840416	CS 1982-2356		19820401
RO 84584	A1	19840717	RO 1982-107118		19820401
PL 130584	B1	19840831	PL 1982-235751		19820401
AT 14429	T	19850815	AT 1982-301739		19820401
DK 8201513	A	19821004	DK 1982-1513		19820402
FI 8201161	A	19821004	FI 1982-1161		19820402
JP 57181079	A	19821108	JP 1982-56481		19820402
ES 511123	A1	19830216	ES 1982-511123		19820402
HU 28746	A2	19831228	HU 1982-1025		19820402
HU 191084	B	19870128			
SU 1138028	A3	19850130	SU 1982-3417251		19820402
PRIORITY APPLN. INFO.:			US 1981-246333	A2	19810403
			US 1981-246335	A	19810403
			US 1981-331045	A	19811216
			US 1981-331046	A	19811216
			EP 1982-301739	A	19820401

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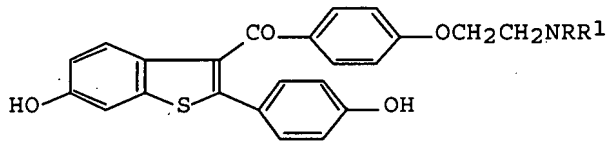

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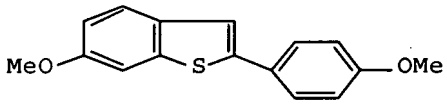

II

AB The acylated benzothiophenones I (R,R1 = C1-4 alkyl, RR1 = polymethylene, CH2CHMeCH2CH2, CH2CH2OCH2CH2) were prepared by acylation-demethylation of benzothiophenes II. Thus, 3-MeOC6H4SN was treated with BrCH2COC6H4OMe-p followed by cyclization to give II, which was treated with AlCl3 and the acid chloride of 4-(2-piperidinoethoxy)benzoic acid to give I (NRR1 = piperidino).

L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1983:71918 CAPLUS Full-text
DOCUMENT NUMBER:	98:71918
TITLE:	Acylated benzothiophenes
INVENTOR(S):	Peters, Mary Kathleen; Jones, Charles David
PATENT ASSIGNEE(S):	Eli Lilly and Co., USA
SOURCE:	Eur. Pat. Appl., 29 pp.
	CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	5
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 62505	A1	19821013	EP 1982-301739		19820401
EP 62505	B1	19850724			
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
US 4380635	A	19830419	US 1981-331046		19811216
AT 14429	T	19850815	AT 1982-301739		19820401
PRIORITY APPLN. INFO.:			US 1981-246333	A	19810403
			US 1981-246335	A	19810403
			US 1981-331045	A	19811216
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			EP 1982-301739	A	19820401

OTHER SOURCE(S): MARPAT 98:71918

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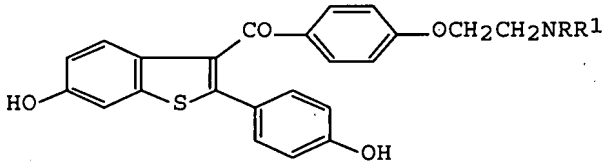

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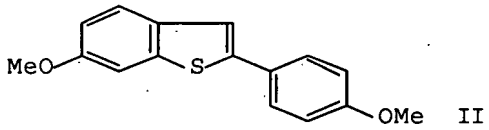

II

AB 3-[4-(2-Aminoethoxy)benzoyl]benzothiophenes I [R, R1 = C1-4 alkyl; RR1 = (CH2)4, (CH2)5, (CH2)6, CH2CHMeCH2CH2, CH2CH2OCH2CH2], useful as antiestrogens (no data), were prepared by acylating benzothiophene II. Thus, heating 3-MeOC6H4SCH2COC6H4OMe-4 with polyphosphoric acid gave II, which was acylated by 4-(Me2NCH2CH2O)C6H4CO2H.HCl and SOCl2 in PhCl-CH2Cl2 containing DMF and AlCl3 to give I (R = R1 = Me).

L6 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:71917 CAPLUS Full-text
DOCUMENT NUMBER: 98:71917
TITLE: Benzothiophene compounds
INVENTOR(S): Jones, Charles David
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 107 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62503	A1	19821013	EP 1982-301737	19820401
R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8282265	A	19821007	AU 1982-82265	19820401

AU 555658	B2	19861002			
GB 2097788	A	19821110	GB 1982-9680		19820401
GB 2097788	B	19850424			
JP 57181081	A	19821108	JP 1982-56479		19820402
PRIORITY APPLN. INFO.:			US 1981-246335	A	19810403
			US 1981-331045	A	19811216

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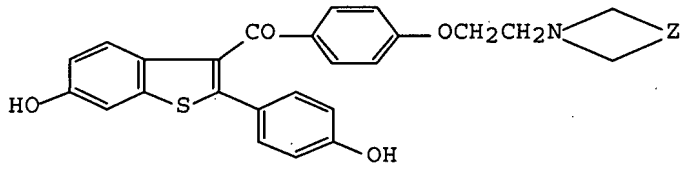

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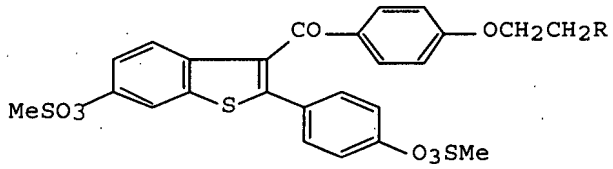

II

AB [(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were prepared, and limited the increase of uterine weight in rats treated with estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).

=>

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NEWS	4	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
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 NEWS  6  MAY 21  TOXCENTER enhanced with BIOSIS reload
 NEWS  7  MAY 21  CA/CAplus enhanced with additional kind codes for German
                  patents
 NEWS  8  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                  patents
 NEWS  9  JUN 27  CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 10  JUN 29  STN Viewer now available
 NEWS 11  JUN 29  STN Express, Version 8.2, now available
 NEWS 12  JUL 02  LEMBASE coverage updated
 NEWS 13  JUL 02  LMEDLINE coverage updated
 NEWS 14  JUL 02  SCISEARCH enhanced with complete author names
 NEWS 15  JUL 02  CHEMCATS accession numbers revised
 NEWS 16  JUL 02  CA/CAplus enhanced with utility model patents from China
 NEWS 17  JUL 16  CAplus enhanced with French and German abstracts
 NEWS 18  JUL 18  CA/CAplus patent coverage enhanced
 NEWS 19  JUL 26  USPATFULL/USPAT2 enhanced with IPC reclassification
 NEWS 20  JUL 30  USGENE now available on STN
 NEWS 21  AUG 06  CAS REGISTRY enhanced with new experimental property tags
 NEWS 22  AUG 06  BEILSTEIN updated with new compounds
 NEWS 23  AUG 06  FSTA enhanced with new thesaurus edition
 NEWS 24  AUG 13  CA/CAplus enhanced with additional kind codes for granted
                  patents
 NEWS 25  AUG 20  CA/CAplus enhanced with CAS indexing in pre-1907 records

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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DICTIONARY FILE UPDATES:  20 AUG 2007  HIGHEST RN 945102-95-4
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=> e raloxifene/cn
E1            1     RALOX LC/CN
E2            1     RALOX-A/CN
E3            1 --> RALOXIFENE/CN
E4            1     RALOXIFENE HYDROCHLORIDE/CN
E5            1     RALOZAM/CN
E6            3     RALSTONITE/CN
E7            1     RALSTONITE (ALF2(OH))/CN
E8            1     RALSTONITE (ALF2(OH).1/2H2O)/CN
E9            1     RALTAT 10/CN
E10           1     RALTEGRAVIR POTASSIUM/CN
E11           1     RALTITREXED/CN
E12           1     RALUBEN/CN

=> s e3
L1            1 RALOXIFENE/CN

=> d l1 1 ide

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   84449-90-1  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-
     piperidinyl)ethoxy]phenyl]-  (CA INDEX NAME)
OTHER NAMES:
CN   Keoxifene
CN   LY 139481
CN   Raloxifene
CN   [2-(4-Hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-(2-(1-
     piperidinyl)ethoxy)phenyl]methanone
MF   C28 H27 N O4 S
CI   COM
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
       BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU,
       DRUGU, EMBASE, HSDB*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA,
       MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, RTECS*, SCISEARCH,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   WHO
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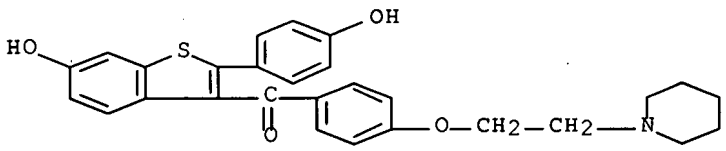

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1751 REFERENCES IN FILE CA (1907 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1763 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

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FILE COVERS 1907 - 21 Aug 2007 VOL 147 ISS 9
FILE LAST UPDATED: 20 Aug 2007 (20070820/ED)

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http://www.cas.org/infopolicy.html

=> s l1
L2 1763 L1

=> d scan

L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 1-0 (Pharmacology)
TI Osteoporosis treatment and limitations and perspectives
ST review bisphosphonate raloxifene parathyroid hormone fall prevention disuse syndrome
IT Bone, disease
(fracture; osteoporosis treatment and limitations and perspectives)
IT Anabolic agents
Osteoporosis
(osteoporosis treatment and limitations and perspectives)

IT Diphosphonates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoporosis treatment and limitations and perspectives)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bisphosphonate; osteoporosis treatment and limitations and perspectives)
IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(osteoporosis treatment and limitations and perspectives)
IT **84449-90-1**, Raloxifene 129318-43-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoporosis treatment and limitations and perspectives)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 1-1 (Pharmacology)
TI Validation of a novel HPLC method for the determination of Raloxifene and its pharmacokinetics in rat plasma
ST Raloxifene detn plasma HPLC; liq chromatog Raloxifene plasma; pharmacokinetics Raloxifene plasma
IT Blood plasma
Pharmacokinetics
(pharmacokinetics of Raloxifene in blood plasma of rats after oral dose)
IT Blood analysis
HPLC
(validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma)
IT **84449-90-1**, Raloxifene
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 1-8 (Pharmacology)
TI Effect of genistein and raloxifene on vascular dependent platelet aggregation
ST genistein raloxifene antiplatelet platelet aggregation blood vessel
IT Blood vessel
Cardiovascular system, disease
Platelet aggregation
Platelet aggregation inhibitors
(effect of genistein and raloxifene on vascular dependent platelet aggregation)
IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)
IT Phytoestrogens
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)

IT 9001-84-7, Phospholipase A2 10102-43-9, Nitric oxide, biological studies
35121-78-9, Prostacyclin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)
IT 446-72-0, Genistein **84449-90-1**, Raloxifene
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of genistein and raloxifene on vascular dependent platelet aggregation)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1/prep
1763 L1
4449106 PREP/RL
L3 38 L1/PREP
(L1 (L) PREP/RL)

=> d l3 4 ibib abs

L3 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1180831 CAPLUS Full-text
DOCUMENT NUMBER: 145:356564
TITLE: The advance of synthetic studies on selective estrogen receptor modulators
AUTHOR(S): Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan
CORPORATE SOURCE: Fourth Brigade of Pharmacy, Medical College of Chinese People's Armed Police Force, Tianjin, 300162, Peop. Rep. China
SOURCE: Wujing Yixueyuan Xuebao (2005), 14(2), 151-156
CODEN: WYXUA9; ISSN: 1008-5041
PUBLISHER: Wujing Yixueyuan Xuebao Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl)stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

=> d l3 ibib abs 1-
YOU HAVE REQUESTED DATA FROM 38 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:70746 CAPLUS Full-text
DOCUMENT NUMBER: 147:172240
TITLE: Control of pharmaceuticals and animal health products in wastewater effluents from manufacturing sites
AUTHOR(S): Parke, Neil J.; Good, Nanci F.; Meyerhoff, Roger D.
CORPORATE SOURCE: Lilly Corporate Center, Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: WEFTEC.05, Conference Proceedings, Annual Technical Exhibition & Conference, 78th, Washington, DC, United States, Oct. 29-Nov. 2, 2005 (2005), 145-155. Water Environment Federation: Alexandria, Va.
CODEN: 69JOAM
DOCUMENT TYPE: Conference; (computer optical disk)

LANGUAGE: English

AB In many cases, the discharge of pharmaceuticals and animal health products at bulk manufacturing, fill/finish, development and research operations may not be directly regulated with numeric limitations as a part of a facility's wastewater discharge permit. The biol. activity of these discharged compds., if not properly managed, may have the potential to impact the operation of an onsite or a municipal wastewater treatment plant, aquatic species in streams, rivers, oceans, or a drinking water source. An overview of the Eli Lilly and Company environmental protection program is provided, which shows how potential releases of active ingredients from its operations are managed to protect the environment.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1063108 CAPLUS Full-text

DOCUMENT NUMBER: 145:417029

TITLE: Methods for generating stably linked complexes composed of homodimers, homotetramers or dimers of dimers

INVENTOR(S): Chien, Hsing Chang; Goldenberg, David M.; McBride, William J.; Rossi, Edmund A.

PATENT ASSIGNEE(S): IBC Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006107617	A2	20061012	WO 2006-US10762	20060324
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007086942	A1	20070419	US 2006-478021	20060629
WO 2007046893	A2	20070426	WO 2006-US25499	20060629
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US 2007087001	A1	20070419	US 2006-581287	20061016

WO 2007047609 A2 20070426 WO 2006-US40431 20061016
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US 2007140966 A1 20070621 US 2006-633729 20061205
WO 2007075270 A2 20070705 WO 2006-US46367 20061205
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PRIORITY APPLN. INFO.:

US 2005-668603P	P	20050406
US 2005-728292P	P	20051019
US 2005-751196P	P	20051216
US 2006-782332P	P	20060314
US 2005-389358	A2	20060324
US 2006-389358	A	20060324
WO 2006-US10762	A	20060324
US 2006-391584	A2	20060328
WO 2006-US12084	A	20060329
US 2005-478021	A2	20060629
US 2006-478021	A	20060629
WO 2006-US25499	A2	20060629
US 2006-864530P	P	20061106

AB The authors disclose dimerization and docking domain (DDD) sequences for the generation of stably tethered structures of defined compns., which may have multiple functionalities and/or binding specificities. The tethered constructs may be virtually any mol. or structure, such as antibodies, antibody fragments, antibody analogs or mimetics, aptamers, binding peptides, fragments of binding proteins, known ligands for proteins or other mols., enzymes, detectable labels or tags, therapeutic agents, toxins, pharmaceuticals, cytokines, interleukins, interferons, radioisotopes, proteins, peptides, peptide mimetics, polynucleotides, RNAi, oligosaccharides, natural or synthetic polymeric substances, nanoparticles, quantum dots, organic or inorg. compds., etc. In one example, a fusion construct of a DDD sequence with an anti-CEA Fd fragment was prepared and shown to target colorectal cancer in a xenograft model.

L3 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:958171 CAPLUS Full-text
DOCUMENT NUMBER: 147:9760
TITLE: Synthesis of raloxifene hydrochloride
AUTHOR(S): Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong,

Ping
CORPORATE SOURCE: Shenyang Institute of Chemical Technology, Faculty of Pharmaceutical-Engineering, Shenyang, 110142, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2005), 14(7), 882-884
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3-methoxybenzenethiol and 4-methoxy-α-bromo acetophenone via five steps, including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

L3 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1180831 CAPLUS Full-text
DOCUMENT NUMBER: 145:356564
TITLE: The advance of synthetic studies on selective estrogen receptor modulators
AUTHOR(S): Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan
CORPORATE SOURCE: Fourth Brigade of Pharmacy, Medical College of Chinese People's Armed Police Force, Tianjin, 300162, Peop. Rep. China
SOURCE: Wujing Yixueyuan Xuebao (2005), 14(2), 151-156
CODEN: WYXUA9; ISSN: 1008-5041
PUBLISHER: Wujing Yixueyuan Xuebao Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl)stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

L3 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:708484 CAPLUS Full-text
DOCUMENT NUMBER: 143:221841
TITLE: Estrogen receptor ligands. Dihydrobenzoxathiin SERAMs with an optimized antagonist side chain
AUTHOR(S): Blizzard, Timothy A.; DiNinno, Frank; Chen, Helen Y.; Kim, Seongkon; Wu, Jane Y.; Chan, Wanda; Birzin, Elizabeth T.; Yang, Yi Tien; Pai, Lee-Yuh; Hayes, Edward C.; DaSilva, Carolyn A.; Rohrer, Susan P.; Schaeffer, James M.; Hammond, Milton L.
CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(17), 3912-3916
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:221841
AB An optimized side chain for dihydrobenzoxathiin SERAMs was discovered and attached to four dihydrobenzoxathiin platforms. The novel SERAMs show

exceptional estrogen antagonist activity in uterine tissue and an MCF-7 breast cancer cell assay.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:451379 CAPLUS Full-text
DOCUMENT NUMBER: 142:487547
TITLE: Antiresorptive mutual salt of raloxifene and bisphosphonic acid
INVENTOR(S): Ha, Tae Hee; Kim, Won Jeoung; Yun, Sangmin; Kim, Cheol Kyung; Kim, Han Kyong; Suh, Kwee-Hyun; Lee, Gwan Sun
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005047282	A1	20050526	WO 2004-KR2954	20041115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2005046883	A	20050519	KR 2003-80494	20031114
EP 1689744	A1	20060816	EP 2004-800095	20041115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 2007082871	A1	20070412	US 2006-579199	20060512
PRIORITY APPLN. INFO.:			KR 2003-80494 A	20031114
			WO 2004-KR2954 W	20041115

OTHER SOURCE(S): MARPAT 142:487547

AB The mutual salt of raloxifene and bisphosphonic acid exhibits unexpectedly synergistic effects of two components to enhance bone mineral d. (BMD), control blood-calcium d., and lower the serum cholesterol level. For example, 3.2 g of alendronic acid was mixed with 5.0 g of raloxifene in 75 mL of ethanol/75 mL of water to obtain 6.5 g of raloxifene alendronate pentahydrate. A soft or hard capsule was prepared containing raloxifene alendronate pentahydrate 30 mg, lactose 215 mg, magnesium stearate 2 mg, and colloidal silica 3 mg. When given to female rats, the mutual salt of raloxifene and alendronic acid markedly enhanced BMD, bone stiffness, trabecular volume and bone volume, and also effectively controlled the blood cholesterol and calcium level through the synergic effects of its two components, as compared with the individual raloxifene hydrochloride or alendronate.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:617920 CAPLUS Full-text
DOCUMENT NUMBER: 142:463529

TITLE: Synthesis of raloxifene hydrochloride
AUTHOR(S): Gong, Ping; Zhao, Yanfang; Wang, Dun
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113
CODEN: SYDXFF; ISSN: 1006-2858
PUBLISHER: Shenyang Yaoke Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 142:463529

AB Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4-hydroxyphenyl)benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3, saponification with 5M NaOH solution in methanol, and saltification with HCl. The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR, 13C NMR.

L3 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:292022 CAPLUS Full-text
DOCUMENT NUMBER: 140:309411
TITLE: Pharmaceutical compositions comprising raloxifene acid addition salts and/or solvates
INVENTOR(S): Karup, Gunnar Leo; Pedersen, Soren Bols
PATENT ASSIGNEE(S): A/S Gea Farmaceutisk Fabrik, Den.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004029046	A2	20040408	WO 2003-DK645	20030930
WO 2004029046	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2499819	A1	20040408	CA 2003-2499819	20030930
AU 2003266940	A1	20040419	AU 2003-266940	20030930
AU 2003266940	B2	20070208		
EP 1546138	A2	20050629	EP 2003-747847	20030930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
NO 2005002100	A	20050629	NO 2005-2100	20050429
US 2006154966	A1	20060713	US 2005-528691	20050921
PRIORITY APPLN. INFO.:			DK 2002-1450 A	20020930
			WO 2003-DK645 W	20030930

OTHER SOURCE(S): MARPAT 140:309411

AB Raloxifene acid addn. salts or solvates thereof, having improved dissoln. properties in media comprising hydrochloric acid are described, compared with similar prepns. based on raloxifene or raloxifene-hydrochloride. The disclosed acid addition salts or solvates thereof show an improved bioavailability in media comprising hydrochloric acid, such as the gastric juice. The acid addition salts or solvates thereof are addition salts or solvates of raloxifene and a pharmaceutically acceptable acid selected among succinic acid, lactic acid, malonic acid or sulfuric acid. Further, crystalline forms of the raloxifene salts and solvates thereof are disclosed. The raloxifene acid addition salts and/or solvates thereof are useful for the preparation of pharmaceutical composition for oral administration capable of fast and reliable release of the active ingredients in the stomach of the patient, in particular for the treatment of cancer or osteoporosis, or for inhibiting cartilage degradation A new method for preparation of raloxifene lactate is also disclosed. Thus, raloxifene malonate was prepared by the reaction of raloxifene-HCl with malonic acid in propanol-water solution The product was characterized by IR spectra and x-ray diffraction.

L3 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:269853 CAPLUS Full-text

DOCUMENT NUMBER: 140:309370

TITLE: Amino acid and peptide carriers for oral delivery of active agent

INVENTOR(S): Piccariello, Thomas; Kirk, Randal J.; Olon, Lawrence P.

PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 176 pp., Cont.-in-part of U.S. Pat. Appl. 2002 128,177.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 24

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004063628	A1	20040401	US 2002-156527	20020529
US 7060708	B2	20060613		
WO 2000052078	A1	20000908	WO 2000-US5693	20000306
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US 6716452	B1	20040406	US 2000-642820	20000822
US 2002099013	A1	20020725	US 2001-933708	20010822
US 2002128177	A1	20020912	US 2001-986426	20011108
US 7018654	B2	20060328		
WO 2003034980	A2	20030501	WO 2001-US43089	20011114
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WO 2002051432 A1 20020704 WO 2001-US43115 20011116

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WO 2003020200 A2 20030313 WO 2001-US43117 20011116

WO 2003020200 A3 20030912

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WO 2003072047 A2 20030904 WO 2003-US5526 20030224

WO 2003072047 A3 20040617

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AU 2003216382 A1 20030909 AU 2003-216382 20030224

CA 2477088 A1 20031002 CA 2003-2477088 20030224

WO 2003079972 A2 20031002 WO 2003-US5524 20030224

WO 2003079972 A3 20040318

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AU 2003217676 A1 20031008 AU 2003-217676 20030224

EP 1490090 A2 20041229 EP 2003-713634 20030224

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CN 1649614 A 20050803 CN 2003-808717 20030224

JP 2005524677 T 20050818 JP 2003-577805 20030224

IN 2003KN00329 A 20041009 IN 2003-KN329 20030320

WO 2003101476 A1 20031211 WO 2003-US17009 20030529

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU	2003240949	A1	20031219	AU	2003-240949	20030529
US	2004127397	A1	20040701	US	2003-727565	20031205
IN	2004KN01318	A	20060616	IN	2004-KN1318	20040908
US	2007066537	A1	20070322	US	2004-953111	20040930
US	2006014697	A1	20060119	US	2005-89056	20050325
US	2007060500	A1	20070315	US	2006-392878	20060330

PRIORITY APPLN. INFO.:

US	1999-265415	B2	19990310
US	1999-411238	B2	19991004
WO	2000-US5693	A	20000306
US	2000-642820	A2	20000822
US	2000-248620P	P	20001116
US	2000-248659P	P	20001116
US	2000-248660P	P	20001116
US	2000-248662P	P	20001116
US	2000-248663P	P	20001116
US	2000-248685P	P	20001116
US	2000-248737P	P	20001116
US	2000-248738P	P	20001116
US	2000-248764P	P	20001116
US	2000-248767P	P	20001116
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US	2000-248774P	P	20001116
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US	2000-248779P	P	20001116
US	2000-248782P	P	20001116
US	2000-248787P	P	20001116
US	2000-248794P	P	20001116
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US	2000-248797P	P	20001116
US	2001-933708	A2	20010822
US	2001-986426	A2	20011108
US	2001-987458	B2	20011114
WO	2001-US43089	B2	20011114
US	2001-988034	B2	20011116
US	2001-988071	B2	20011116
WO	2001-US43115	B2	20011116
WO	2001-US43117	B2	20011116
US	2002-358381P	P	20020222
US	2002-366258P	P	20020322
US	1999-123146P	P	19990305
US	2000-247556P	P	20001114
US	2000-247558P	P	20001114
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US 2000-247560P	P	20001114
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US 2000-247610P	P	20001114
US 2000-247611P	P	20001114
US 2000-247612P	P	20001114
US 2000-247620P	P	20001114
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US 2000-247702P	P	20001114
US 2000-247797P	P	20001114
US 2000-247798P	P	20001114
US 2000-247799P	P	20001114
US 2000-247800P	P	20001114
US 2000-247801P	P	20001114
US 2000-247802P	P	20001114
US 2000-247803P	P	20001114
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US 2000-247807P	P	20001114
US 2000-247832P	P	20001114
US 2000-247833P	P	20001114
US 2000-247926P	P	20001114
US 2000-247927P	P	20001114
US 2000-247928P	P	20001114
US 2000-247929P	P	20001114
US 2000-247930P	P	20001114
US 2000-274622P	P	20001114
US 2000-248528P	P	20001116
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US 2000-248601P	P	20001116
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US 2000-248693P	P	20001116
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US 2000-248702P	P	20001116

US 2000-248703P	P	20001116
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US 2000-248709P	P	20001116
US 2000-248710P	P	20001116
US 2000-248711P	P	20001116
US 2000-248712P	P	20001116
US 2000-248733P	P	20001116
US 2000-248748P	P	20001116
US 2001-959396	B2	20011024
US 2002-358368P	P	20020222
US 2002-362082P	P	20020307
US 2002-136433	A	20020502
US 2002-156527	A	20020529
WO 2003-US5524	W	20030224
WO 2003-US5525	A2	20030224
WO 2003-US5526	W	20030224
WO 2003-US17009	W	20030529
US 2003-507012P	P	20030930
US 2004-567800P	P	20040505
US 2004-567802P	P	20040505
US 2004-568011P	P	20040505
US 2004-923088	A2	20040823
US 2004-923257	A2	20040823
US 2004-953110	A2	20040930
US 2004-953111	A2	20040930
US 2004-953116	A2	20040930
US 2004-953119	A2	20040930
US 2004-955006	A2	20040930
WO 2004-US32131	A2	20040930

AB The present invention relates to oral delivery systems of active agent, and more specifically to compns. that comprise amino acids, as single amino acids or peptides, covalently attached to active agents and methods for oral administration of conjugated active agent compns. For example, a polyserine-furosemide conjugate was prepared and its in vivo performance was examined Compared to parent furosemide, the conjugate showed a sustained drug release. The 9 h serum level of the polyserine-furosemide conjugate was 95.5% of its 3 h level, whereas the 9 h serum level of the parent drug was only 59.8% of its 3 h level.

L3 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:726588 CAPLUS Full-text
DOCUMENT NUMBER: 139:345292

TITLE: Nitrosation, nitration, and autoxidation of the selective estrogen receptor modulator raloxifene by nitric oxide, peroxynitrite, and reactive nitrogen/oxygen species

AUTHOR(S): Toader, Violeta; Xu, Xudong; Nicolescu, Adrian; Yu, Linning; Bolton, Judy L.; Thatcher, Gregory R. J.
CORPORATE SOURCE: Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, 60612-7231, USA

SOURCE: Chemical Research in Toxicology (2003), 16(10), 1264-1276
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The regulation of estrogenic and antiestrogenic effects by selective estrogen receptor modulators (SERMs) provides the basis for use in long-term therapy in cancer chemoprevention and postmenopausal osteoporosis. However, the evidence for carcinogenic properties within this class requires study of potential pathways of toxicity. There is strong evidence for the elevation of cellular levels of NO in tissue treated with SERMs, including the benzothiophene derivative, raloxifene, in part via up-regulation of nitric oxide synthases. Therefore, the reactions of 17β-estradiol (E2), raloxifene, and an isomer with NO, peroxynitrite, and reactive nitrogen/oxygen species (RNOS) generated from NO2-/H2O2 systems were examined Peroxynitrite from bolus injection or slow release from higher concns. of 3-morpholinosydnonimine (SIN-1) reacted with the benzothiophenes and E2 to give aromatic ring nitration, whereas peroxynitrite, produced from the slow decomposition of lower concns. of SIN-1, was relatively unreactive toward E2 and yielded oxidation and nitrosation products with raloxifene and its isomer. The oxidation and nitrosation products formed were characterized as a dimer and quinone oxime derivative Interestingly, the reaction of the benzothiophenes with NO in aerobic solution efficiently generated the same oxidation products. Stable quinone oximes are not unprecedented but have not been previously reported as products of RNOS-mediated metabolism The reaction of glutathione (GSH) with the quinone oxime gave both GSH adducts from Michael addition and reduction to the corresponding o-aminophenol. The ready autoxidn. of raloxifene, observed in the presence of NO, is the first such observation on the reactivity of SERMs and is potentially a general phenomenon of significance to SERM chemical toxicol.

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:491620 CAPLUS Full-text
DOCUMENT NUMBER: 139:179942
TITLE: Synthesis of Constrained Raloxifene Analogues by Complementary Use of Friedel-Crafts and Directed Remote Metalation Reactions
AUTHOR(S): Kalinin, Alexey V.; Reed, Mark A.; Norman, Bryan H.; Snieckus, Victor
CORPORATE SOURCE: Department of Chemistry, Queen's University, Kingston, ON, K7L 3N6, Can.
SOURCE: Journal of Organic Chemistry (2003), 68(15), 5992-5999
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:179942
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB New constrained heterocyclic analogs of Raloxifene, I [R1 = 2-(1-piperidinyl)ethoxy, R2 = H; R1 = H, R2 = 2-(1-piperidinyl)ethoxy] and II, were prepared by complementary Directed remote Metalation (DreM)/Friedel-Crafts cyclization approaches. Utilization of a benzylidene-thiolactone rearrangement was successfully implemented to construct benzothiophenes III (R3 = Me2CH, R4 = MeO; R3 = Me, PhCH2, R4 = Et2N) in good yields. Selective deprotection of III (R3 = Me2CH, R4 = MeO; R3 = PhCH2, R4 = Et2N) induced by complexation was followed by trifluoromethylsulfonylation and Suzuki-Miyaura

cross coupling with 3-[2-(1-piperidinyl)ethoxy]phenyl dioxaborolane to give the corresponding 2,4-diaryl-substituted benzothiophenes with methoxycarbonyl or diethylcarbamoyl group in the 3 position. Treatment of the latter with BCl3 or with excess LDA induced an intramol. para or ortho cyclization and concomitant double deprotection to furnish I. Similar sequence starting from III (R3 = Me, R4 = Et2N) afforded the constrained analog II.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:408662 CAPLUS Full-text

DOCUMENT NUMBER: 136:401637

TITLE: Preparation of 3-arylbenzothiophenes by cyclodehydration of phenylthioacetophenones using activated clay or zeolite catalysts.

INVENTOR(S): Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

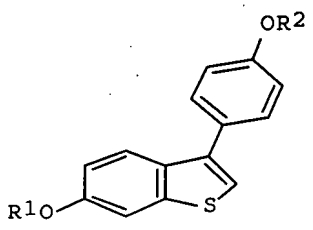
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042289	A2	20020530	WO 2001-US42940	20011114
WO 2002042289	A3	20020906		
WO 2002042289	A8	20040212		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002030409	A5	20020603	AU 2002-30409	20011114
US 2004132775	A1	20040708	US 2003-415569	20030922
US 6921827	B2	20050726		

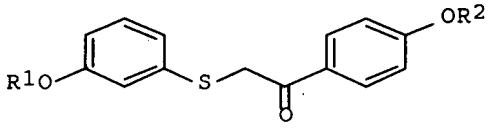
PRIORITY APPLN. INFO.: US 2000-253212P P 20001127
WO 2001-US42940 W 20011114

OTHER SOURCE(S): CASREACT 136:401637; MARPAT 136:401637

GI



I



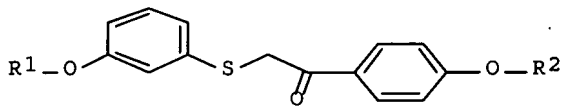
II

AB Title compds. (I; R1, R2 = H, protecting group) were prepd. by cyclodehydration of phenylthioacetophenones (II; variables as above) in the presence of acid activated clays or acid activated zeolites and in the presence of solvents. Thus, PhMe, α-(3-methoxyphenylthio)-4-methoxyacetophenone, and "acid-activated clay" (Engelhard X-9107) were combined and refluxed 2 h using a Dean Stark trap. By HPLC the product mixture consisted of 96.7% 6-methoxy-3-(4-methoxyphenyl)benzo[b]thiophene, 1.1% 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene, 2.1% 4-methoxy-3-(4-methoxyphenyl)benzo[b]thiophene, and 0.1% 4-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene.

L3 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:408636 CAPLUS Full-text
DOCUMENT NUMBER: 136:401533
TITLE: Coupling reaction process for preparing α-(3-arylthio)acetophenones from thiophenol derivs. and α-(leaving group)-substituted acetophenones
INVENTOR(S): Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042261	A2	20020530	WO 2001-US42939	20011114
WO 2002042261	A3	20030306		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002028593	A5	20020603	AU 2002-28593	20011114
PRIORITY APPLN. INFO.:			US 2000-253073P P	20001127
			WO 2001-US42939 W	20011114

OTHER SOURCE(S): CASREACT 136:401533; MARPAT 136:401533
GI



I

AB α-(3-Arylthio)acetophenones [I; R1, R2 = H, hydroxy-protecting group; e.g., α-(3-methoxyphenylthio)-4-methoxyacetophenone] are prepared in high yield and

selectivity by the coupling of a thiophenol derivative 3-(R1O)C6H4SH (e.g., 3-methoxybenzenethiol) in an aqueous alkaline (e.g., KOH) solvent (e.g., Et acetate) with an aromatic ketone LCH2COC6H4(OR2)-4 (L = leaving group; e.g., α-chloro-4-methoxyacetophenone).

L3 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:283971 CAPLUS Full-text
DOCUMENT NUMBER: 134:300772
TITLE: Glycosides and orthoester glycosides of raloxifene and analogues and the use thereof
INVENTOR(S): Holick, Michael Francis; Ramanathan, Halasya
PATENT ASSIGNEE(S): Strakan Group PLC, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001027129	A1	20010419	WO 2000-GB3864		20001006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
GB 2355007	A	20010411	GB 1999-28100		19991126
PRIORITY APPLN. INFO.:			US 1999-158141P	P	19991008
			US 2000-231573P	P	20000911

OTHER SOURCE(S): MARPAT 134:300772
AB Raloxifene and raloxifene analog glycosides and orthoester glycosides afford greater serum bioavailability of the hydroxylated parent compound, and are useful for treating or preventing a number of conditions that may be treated with an anti-estrogenic or an anti-androgenic compound To a mixture of 0.5 g raloxifene and 1.6 g silver silicate in dry acetonitrile was added 3 g mol. sieves and stirred for 20 min. To the above suspension was added 1.0 g acetobromo-α-D-glucose and heated for 2 h at 60°, then filtered through a bed of silica gel and eluted with dichloromethane and methanol. The yellow eluent was concentrated under vacuum to obtain yellowish crystals. Proton NMR spectrum showed the crystals were consisted of 2 possible monoglucosides and a doubly glycosylated product.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:440767 CAPLUS Full-text
DOCUMENT NUMBER: 131:228604
TITLE: Synergistic methodologies for the synthesis of 3-aroyl-2-arylbenzo[b]thiophene-based selective estrogen receptor modulators. Two concise syntheses of raloxifene
AUTHOR(S): Bradley, David A.; Godfrey, Alexander G.; Schmid, Christopher R.
CORPORATE SOURCE: Chemical Process Research and Development, A Division

of Eli Lilly and Company, Lilly Corporate Center, Lilly Research Laboratories, Indianapolis, IN, 46285-4813, USA
SOURCE: Tetrahedron Letters (1999), 40(28), 5155-5159
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Functionalized benzo[b]thiophene intermediates are prepd. which allow fully independent elaboration of the 2-aryl position or the tether position of benzo[b]thiophene-based selective estrogen receptor modulators (SERMs). Two concise syntheses of the SERM raloxifene (Evista) are presented.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:188589 CAPLUS Full-text
DOCUMENT NUMBER: 130:311683
TITLE: Novel nonsteroidal selective estrogen receptor modulators. Carbon and heteroatom replacement of oxygen in the ethoxypiperidine region of raloxifene
AUTHOR(S): Schmid, Christopher R.; Sluka, James P.; Duke, Kristen M.; Glasebrook, Andrew W.
CORPORATE SOURCE: Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(4), 523-528
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Compds. were synthesized where oxygen in the ethoxypiperidine region of raloxifene is replaced with carbon, sulfur, or nitrogen linkages. Thia- and aza-substituted compds. were prepared by novel methodol. The compds. were evaluated in vitro as selective estrogen receptor modulators (SERMs). Calcns. suggested the compds. exhibit an ER-α binding affinity/conformational energy relationship.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:71534 CAPLUS Full-text
DOCUMENT NUMBER: 130:196550
TITLE: Nucleophilic aromatic substitution on 3-aroyl-2-arylbenzothiophenes. Rapid access to raloxifene and other selective estrogen receptor modulators
AUTHOR(S): Schmid, Christopher R.; Sluka, James P.; Duke, Kristin M.
CORPORATE SOURCE: Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285-4813, USA
SOURCE: Tetrahedron Letters (1999), 40(4), 675-678
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:196550

AB Versatile, mild and high yielding methods for nucleophilic arom. substitution of 2-dialkylamino-1-ethoxides and related nucleophiles on 3-aroyl-2-arylbenzothiophene nuclei are presented. A short synthesis of raloxifene is detailed.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:721690 CAPLUS Full-text

DOCUMENT NUMBER: 130:3769

TITLE: Processes for preparing benzothiophenes

INVENTOR(S): McGill, John McNeil, III; Misner, Jerry Wayne; Zhang, Tony Yantao

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849156	A1	19981105	WO 1998-US8509	19980428
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2287943	A1	19981105	CA 1998-2287943	19980428
AU 9872613	A	19981124	AU 1998-72613	19980428
BR 9809439	A	20000613	BR 1998-9439	19980428
HU 200003187	A2	20010528	HU 2000-3187	19980428
JP 2001522372	T	20011113	JP 1998-547277	19980428
US 6090949	A	20000718	US 1998-69497	19980429
EP 875510	A1	19981104	EP 1998-303374	19980430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
MX 9909883	A	20000331	MX 1999-9883	19991027

PRIORITY APPLN. INFO.: US 1997-45177P P 19970430
WO 1998-US8509 W 19980428

OTHER SOURCE(S): CASREACT 130:3769; MARPAT 130:3769

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y = Cl, Br, I, SO2(C1-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = C1-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.

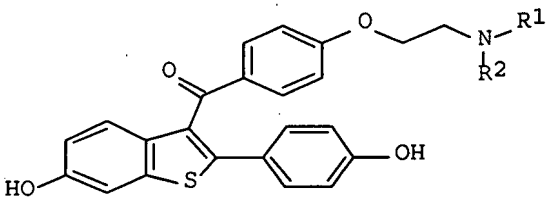
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:721501 CAPLUS Full-text
DOCUMENT NUMBER: 130:3768
TITLE: Demethylation process for preparing benzo[b]thiophenes
INVENTOR(S): Hoard, David Warren; Luke, Wayne Douglas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 875511	A1	19981104	EP 1998-303345		19980429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CA 2236254	A1	19981030	CA 1998-2236254		19980427
JP 11005789	A	19990112	JP 1998-118628		19980428
US 5994547	A	19991130	US 1998-69500		19980429
PRIORITY APPLN. INFO.:			US 1997-45156P	P	19970430

OTHER SOURCE(S): CASREACT 130:3768; MARPAT 130:3768
GI



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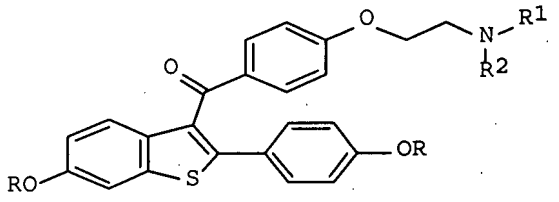

II

AB The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2-methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be carried out in the same reaction vessel without isolation of the acylated, protected material.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:719257 CAPLUS Full-text
DOCUMENT NUMBER: 130:3765
TITLE: Intermediates and processes for preparing

benzo[b]thiophenes
INVENTOR(S): Misner, Jerry Wayne; Schmid, Christopher Randall
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9848793	A1	19981105	WO 1998-US8510		19980428
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2287922	A1	19981105	CA 1998-2287922		19980428
AU 9872614	A	19981124	AU 1998-72614		19980428
EP 979076	A1	20000216	EP 1998-919936		19980428
R: AT, BE, DE, DK, ES, FR, GB, GR, IT, NL, SE, PT, IE, FI					
JP 2001523253	T	20011120	JP 1998-547278		19980428
US 6018056	A	20000125	US 1998-69278		19980429
PRIORITY APPLN. INFO.:			US 1997-45131P	P	19970430
			WO 1998-US8510	W	19980428

OTHER SOURCE(S): CASREACT 130:3765; MARPAT 130:3765
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I-III; R = hydroxy protecting group; Y = CO2H, CO2(C1-4 alkyl), C(halo), etc.; A = OH, halo, NO2, etc.; R1 = hydroxy protecting group, H], useful intermediates in the further preparation of pharmaceutical benzo[b]thiophenes, were prepared Thus, reaction of 6-methoxythianaphthen-2-one with p-anisaldehyde in the presence of piperidine in EtOH and THF afforded 45% E/Z-I [R = Me].
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:161136 CAPLUS Full-text
DOCUMENT NUMBER: 128:221639
TITLE: Preparation of amorphous benzothiophenes for pharmaceuticals
INVENTOR(S): Cuff, George W.; Thakkar, Arvind L.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Cuff, George W.; Thakkar, Arvind L.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9808513	A1	19980305	WO 1997-US14768		19970822
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
EP 826682	A1	19980304	EP 1997-306426		19970822
EP 826682	B1	20030312			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CA 2263175	A1	19980305	CA 1997-2263175		19970822
AU 9742335	A	19980319	AU 1997-42335		19970822
AU 723987	B2	20000907			
IN 182940	A1	19990814	IN 1997-CA1549		19970822
BR 9713176	A	20000208	BR 1997-13176		19970822
CN 1244124	A	20000209	CN 1997-197434		19970822
HU 200001172	A2	20010628	HU 2000-1172		19970822
HU 200001172	A3	20020128			
NZ 333839	A	20010629	NZ 1997-333839		19970822
IL 128641	A	20011031	IL 1997-128641		19970822
TR 9900403	T2	20020121	TR 1999-403		19970822
JP 2002514174	T	20020514	JP 1998-511744		19970822
AT 234295	T	20030315	AT 1997-306426		19970822
ES 2195089	T3	20031201	ES 1997-306426		19970822
ZA 9707617	A	19990225	ZA 1997-7617		19970825
US 6713494	B1	20040330	US 1997-918741		19970825
NO 9900914	A	19990225	NO 1999-914		19990225
KR 2000035941	A	20000626	KR 1999-701682		19990227
PRIORITY APPLN. INFO.:			US 1996-24831P	P	19960828
			WO 1997-US14768	W	19970822

OTHER SOURCE(S): MARPAT 128:221639

AB A method for prepg. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 38 CAPLUS

ACCESSION NUMBER: 1997:589698 CAPLUS Full-text

DOCUMENT NUMBER: 127:272904

TITLE: Evaluation of piperidinoethoxy moiety as an antiestrogenic substituent in non-steroidal anti-estrogens: fertility regulation

AUTHOR(S): Tripathi, Sachi; Dwivedy, Indra; Dhar, J. D.; Dwivedy, Anila; Ray, Suprabhat

CORPORATE SOURCE: Medicinal Chemistry Division, Central Drug Research Institute, Lucknow, 226 001, India

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(16), 2131-2136
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A piperidinoethoxy substituent in non-steroidal antiestrogens has a relatively higher antiestrogenic effect as compared to a pyrrolidinoethoxy moiety. However, the antagonistic activity is more depended on the mol. geometry than the nature of the basic chain. No significant difference in the antifertility activity in these two sets of compds. was observed

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:124440 CAPLUS Full-text

DOCUMENT NUMBER: 126:144105

TITLE: Preparation of 3-phenylbenzo[b]thiophenes

INVENTOR(S): Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Hoard, David W.; Luke, Wayne D.

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640677	A1	19961219	WO 1996-US9477	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5606075	A	19970225	US 1995-481015	19950607
CA 2223709	A1	19961219	CA 1996-2223709	19960604
AU 9661010	A	19961230	AU 1996-61010	19960604
AU 703017	B2	19990311		
EP 830355	A1	19980325	EP 1996-918320	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192738	A	19980909	CN 1996-196109	19960604
BR 9608851	A	19990608	BR 1996-8851	19960604
JP 11507347	T	19990629	JP 1996-501787	19960604
HU 9900898	A2	19990728	HU 1999-898	19960604
HU 9900898	A3	20000228		
EP 1092714	A2	20010418	EP 2000-128207	19960604
EP 1092714	A3	20010704		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
IL 122128	A	20010808	IL 1996-122128	19960604
NO 9705627	A	19980127	NO 1997-5627	19971204

PRIORITY APPLN. INFO.:

US 1995-481015	A	19950607
EP 1996-918320	A3	19960604
WO 1996-US9477	W	19960604

OTHER SOURCE(S): MARPAT 126:144105

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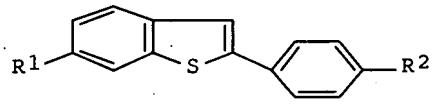

I

AB Title compds. [I; R1,R2 = H, halo, (aryl)alkoxy, NH2] were pred. by cyclization of 4-R1C6H4CH:C(SR4)C6H4R2-4 [R4 = trialkylsilyloxy, (di)(alkyl)amino, alkylthio, etc.] in the presence of an acid.

L3 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:740256 CAPLUS Full-text
DOCUMENT NUMBER: 126:7985
TITLE: Preparation of 3-[4-(2-heterocyclylethoxy)benzoyl-2-phenylbenzothiophenes for use in alleviating the symptoms of post-menopausal syndrome
INVENTOR(S): Dodge, Jeffrey Alan; Jones, Charles David; Bourgeois, Tokarz Michelle Lee
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 67 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 738725	A2	19961023	EP 1996-302713		19960418
EP 738725	A3	19970305			
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, NL, PT, SE					
US 6608090	B1	20030819	US 1995-426552		19950421
CA 2215902	A1	19961024	CA 1996-2215902		19960418
WO 9632937	A1	19961024	WO 1996-US5382		19960418
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ					
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9655549	A	19961107	AU 1996-55549		19960418
JP 11504013	T	19990406	JP 1996-531911		19960418
PRIORITY APPLN. INFO.:			US 1995-426339	A	19950421
			US 1995-426552	A	19950421
			WO 1996-US5382	W	19960418

OTHER SOURCE(S): MARPAT 126:7985
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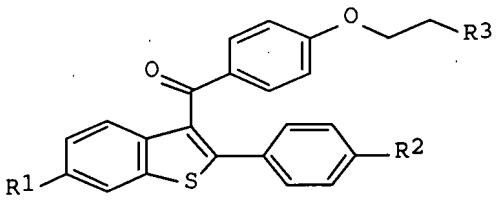

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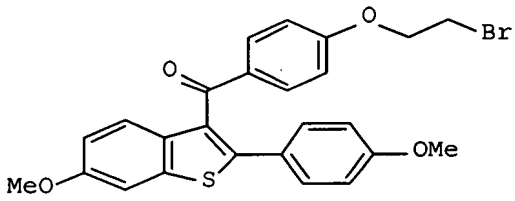

II

AB The title compds. [I; R1, R2 = H, OH, alkoxy, etc.; R3 = (substituted) pyrrolidino, piperidino, piperazino, etc.], useful in alleviating the symptoms of post-menopausal syndrome related to osteoporosis, cardiovascular disease, hyperlipidemia, estrogen-dependent cancer, and in alleviating the symptoms of uterine fibroid disease, endometriosis, aortal smooth muscle cell proliferation, and restenosis, were prepared and formulated. Thus, reaction of bromide II with 3-phenylpyrrolidine in DMF followed by demethylation with EtSH/AlCl3 in CH2Cl2 afforded I [R1, R2 = H; R3 = 3-Ph-pyrrolidin-1-yl] which reduced 63.4% serum cholesterol at 10 mg/kg.

L3 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:672963 CAPLUS Full-text
DOCUMENT NUMBER: 126:7983
TITLE: Process for the synthesis of benzo[b]thiophenes
INVENTOR(S): Hoard, David W.; Luke, Wayne D.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5569772	A	19961029	US 1995-486873	19950607
CA 2223681	A1	19961219	CA 1996-2223681	19960604
WO 9640678	A1	19961219	WO 1996-US9357	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9660970	A	19961230	AU 1996-60970	19960604
AU 698558	B2	19981029		
EP 830356	A1	19980325	EP 1996-918277	19960604
EP 830356	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,				

SI, LT, LV, FI

CN 1192212	A	19980902	CN 1996-195899		19960604
BR 9609156	A	19990629	BR 1996-9156		19960604
JP 11507338	T	19990629	JP 1997-501694		19960604
HU 9900903	A2	19990728	HU 1999-903		19960604
HU 9900903	A3	20010129			
IL 122091	A	20010520	IL 1996-122091		19960604
AT 204575	T	20010915	AT 1996-918277		19960604
ES 2159742	T3	20011016	ES 1996-918277		19960604
PT 830356	T	20011228	PT 1996-918277		19960604
NO 9705579	A	19971203	NO 1997-5579		19971203
PRIORITY APPLN. INFO.:			US 1995-486873	A	19950607
			WO 1996-US9357	W	19960604

OTHER SOURCE(S): CASREACT 126:7983; MARPAT 126:7983

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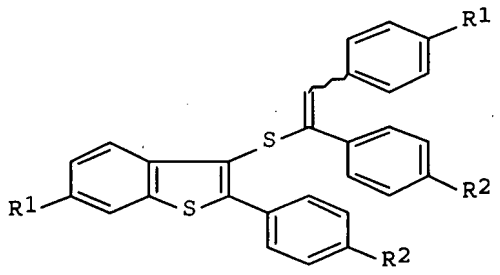

I

AB The title compds. I [R1, R2 = H, alkoxy, etc.] are prepd. Thus, treatment of (E)-tert-Bu 4,4'-dimethoxystilbenyl sulfoxide with p-toluenesulfonic acid in refluxing toluene gave, after workup and purifn, (E)- and (Z)-I [R1 = R2 = MeO].

L3 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:649600 CAPLUS Full-text

DOCUMENT NUMBER: 125:266032

TITLE: Phosphorous-containing benzothiophenes, their preparation, their use in treating postmenopausal syndrome-associated indications and estrogen-dependent diseases, and pharmaceuticals containing them

INVENTOR(S): Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey S.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 729964	A1	19960904	EP 1996-300878	19960209
EP 729964	B1	20010509		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE

US 6479517	B1	20021112	US 1995-395944	19950228
ES 2158242	T3	20010901	ES 1996-300878	19960209
CA 2169414	A1	19960829	CA 1996-2169414	19960213
JP 08259560	A	19961008	JP 1996-25281	19960213
US 5998443	A	19991207	US 1997-946842	19971008

PRIORITY APPLN. INFO.: US 1995-395944 A 19950228
OTHER SOURCE(S): MARPAT 125:266032
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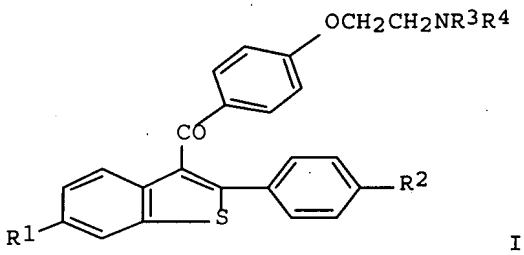


I

AB Phosphorus-contg. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(O-alkyl)2, OPO(O-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3-dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds. of the invention, as well as pharmaceutical compns. containing compds. of the invention.

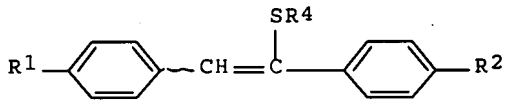
L3 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:333087 CAPLUS Full-text
DOCUMENT NUMBER: 125:86485
TITLE: Prepn. of vinyl sulfenic acid derivatives for benzo[b]thiophene synthesis
INVENTOR(S): Hoard, David W.; Luke, Wayne D.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5514826	A	19960507	US 1995-483607	19950607
CA 2224225	A1	19961219	CA 1996-2224225	19960604
WO 9640693	A1	19961219	WO 1996-US9460	19960604

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM

AU 9661003	A	19961230	AU 1996-61003		19960604
AU 698076	B2	19981022			
EP 830362	A1	19980325	EP 1996-918314		19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI					
CN 1192215	A	19980902	CN 1996-195947		19960604
CN 1068883	B	20010725			
BR 9608847	A	19990608	BR 1996-8847		19960604
JP 11507346	T	19990629	JP 1997-501774		19960604
HU 9900923	A2	19990728	HU 1999-923		19960604
HU 9900923	A3	20000228			
IL 122127	A	20010520	IL 1996-122127		19960604
NO 9705633	A	19980128	NO 1997-5633		19971204
CN 1330071	A	20020109	CN 2000-130796		20001212
PRIORITY APPLN. INFO.:			US 1995-482692	A	19950607
			US 1995-483607	A	19950607
			WO 1996-US9460	W	19960604

GI



I

AB The present invention is directed to novel vinyl sulfenic acid derivs. I [R1, R2 = H, alkoxy, arylalkoxy, halo, amino; R4 = OSi(R3)3, NR5R6, SR8; R5and/or R6 = H, alkyl, arylalkyl, aryl, -(CH2)5-, -(CH2)4-, -(CH2)2O(CH2)2-, -(CH2)6-; R8 = alkyl, aryl, arylalky] useful for the synthesis of benzo[b]thiophenes, in particular 2-arylbenzo[b]thiophenes. E.g., desoxyanisoin reacts with 2-methyl-2-propanethiol to give I [R1 = R2 = OMe; R4 = C(Me)3] which in turn cyclizes to 6-methoxy-2-(4- methoxyphenyl)benzo[b]thiophene.

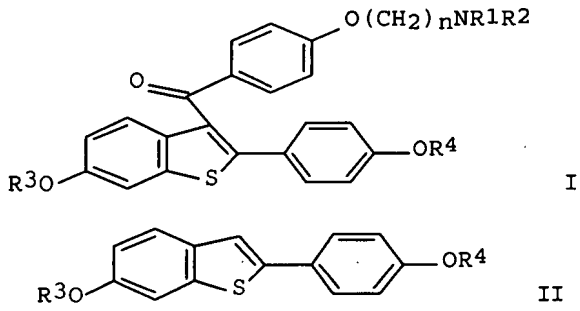
L3 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:256454 CAPLUS Full-text
DOCUMENT NUMBER: 124:289252
TITLE: Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceutical agents
INVENTOR(S): Kjell, Douglas Patton
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 699673	A1	19960306	EP 1995-306053	19950830

EP 699673		B1	19980422			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE						
US 5731436		A	19980324	US 1994-298891		19940831
IL 115091		A	20000831	IL 1995-115091		19950828
IL 126593		A	20000831	IL 1995-126593		19950828
CA 2157235		A1	19960301	CA 1995-2157235		19950830
FI 9504068		A	19960301	FI 1995-4068		19950830
HU 73136		A2	19960628	HU 1995-2539		19950830
BR 9503847		A	19960917	BR 1995-3847		19950830
AT 165356		T	19980515	AT 1995-306053		19950830
ES 2114722		T3	19980601	ES 1995-306053		19950830
JP 08119912		A	19960514	JP 1995-223184		19950831
US 5955608		A	19990921	US 1998-16761		19980130
PRIORITY APPLN. INFO.:				US 1994-298891	A	19940831
				IL 1995-115091	A3	19950828

OTHER SOURCE(S): MARPAT 124:289252

GI



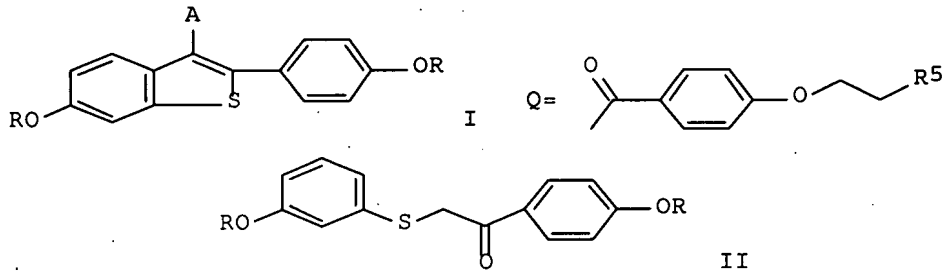
AB The present invention provides a novel process for prepg. a compd. of formula RO2C(p-C6H4)O(CH2)nNR1R2 [R = C1-C4 alkyl; R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino, morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3]; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2(p-C6H4)O(CH2)nOH [R and n are as defined above, with a leaving group donor]; and (c) reacting the product of step (b), a compound of formula RO2(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneamine]. The product of the above process also is novel and is useful for the preparation of pharmaceutically active compds. of formula I, particularly via the following novel process [R = C1-C4 alkyl; R1 and R2 each are independently C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino, morpholino, dimethylamino, diethylamino, of 1-hexamethyleneimino; n = 2, 3]; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2C(p-C6H4)O(CH2)nOH [R and n are as defined above, with the leaving group donor]; (c) reacting the product of step (b), a compound of formula RO2C(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group

with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneimine]; (d) reacting the product of step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing the reaction product from step (d); and (f) optionally forming a salt of the reaction product from either step (d) or step (e).

L3 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:237478 CAPLUS Full-text
DOCUMENT NUMBER: 124:289249
TITLE: An improved process for preparing 3-(4-aminoethoxybenzoyl)benzo[b]thiophenes
INVENTOR(S): Alt, Charles Arthur
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 693488	A1	19960124	EP 1995-305085		19950720
EP 693488	B1	20010919			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
US 5523416	A	19960604	US 1995-422294		19950414
HU 71596	A2	19960129	HU 1995-2176		19950719
AU 9525068	A	19960201	AU 1995-25068		19950719
AU 684181	B2	19971204			
ZA 9506031	A	19970120	ZA 1995-6031		19950719
CA 2154319	A1	19960123	CA 1995-2154319		19950720
FI 9503513	A	19960123	FI 1995-3513		19950720
NO 9502891	A	19960123	NO 1995-2891		19950720
CN 1116624	A	19960214	CN 1995-109618		19950720
JP 08053440	A	19960227	JP 1995-183923		19950720
IL 114684	A	19990620	IL 1995-114684		19950720
AT 205842	T	20011015	AT 1995-305085		19950720
ES 2160668	T3	20011116	ES 1995-305085		19950720
PT 693488	T	20020228	PT 1995-305085		19950720
BR 9503408	A	19960227	BR 1995-3408		19950721
US 5512684	A	19960430	US 1995-512724		19950808
PRIORITY APPLN. INFO.:			US 1994-279456	A	19940722
			US 1995-422294	A1	19950414

OTHER SOURCE(S): CASREACT 124:289249; MARPAT 124:289249
GI



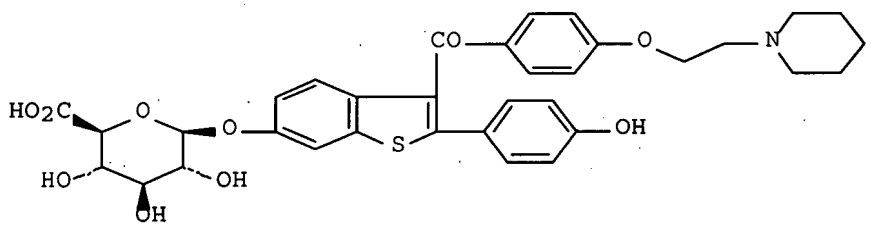
AB A process for prepg. 6-alkoxy-3-(4-alkoxyphenyl)benzo[b]thiophenes (I; A = H; R = same or different C1-6 alkyl) in good yield on a manufacturing scale without generating a thick, potentially yield-reducing, paste and thereby without mixing problems, involves intramol. cyclization of α-(3-alkoxyphenylthio)-4-alkoxyacetophenones (II; R = same as above). The invention also provides methods for converting α-(alkoxyphenylthio)-4-alkoxyacetophenones I (A = H; R = same as above) into 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2- aminoethoxy)benzoyl]benzo[B]thiophenes I (A = Q, R = H; R5 = NR1R2; wherein R1, R2 = C1-4 alkyl, or R1R2 = C4-6 polymethylene or CH2CH2OCH2CH2) via acylation of a dialkoxy benzo[b]thiophene I (A = H; R = same as above) with an acylating agent R4-Q (R4 = Cl, Br, an active ester, etc.; R5 = same as above) under Friedel-Crafts conditions. Thus, 164 g α-bromo-4-methoxyacetophenone was added portion-wise to a mixture of 100 g 4-methoxybenzenethiol and 39 g KOH in 300 mL and denatured EtOH in a cooling and stirred for 10 min in the cooling bath and at ambient temperature for 3 h to give, after workup, 158 g α-(3-methoxyphenylthio)-4- methoxyacetophenone. The latter compound (6.92 g) was added steadily over 1/2 h to a mixture of 41.5 g polyphosphoric acid and 13.8 g phosphoric acid and the reaction mixture was heated at 85° for 1.75 h and cooled to 50°, to give , after extraction with toluene and crystallization, the desired 6-isomer, I (A = H, R = Me)(69% yield). The latter compound (30 g) was heated with 90 g pyridine hydrochloride with stirring at 210° for 30 min to give, after workup, 25.5 g I (A = R = H), which (40 g) was acetylated by Ac2O in the presence of 4-dimethylaminopyridine in pyridine to give 52.5 g I (A = H, R = Ac). This compound (20 g) was added to a solution of 4-(2-piperidinoethoxy)benzoyl chloride (prepared from 16.3 g of the benzoic acid derivative) in ClCH2CH2Cl and stirred vigorously, followed by adding 73.4 g AlCl3 over 3 min, and the resulting mixture was stirred for 1 h to give, after workup, the desired product I [A = Q (wherein R5 = piperidino), R = Ac] as an oil, which was saponified with a mixture of 275 mL MeOH and 55 mL 5 n aqueous NaOH under reflux to give 10.5 g the title compound I [A = Q, wherein R5 = piperidino, R = H].

L3 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:150242 CAPLUS Full-text
DOCUMENT NUMBER: 124:202950
TITLE: Preparation of benzothiophene glucopyranosides as antihyperlipidemics.
INVENTOR(S): Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom, Terry Donald; Lugar, Charles Willis Iii; Staten, Gilbert Stanley
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 683170	A1	19951122	EP 1995-303265	19950516
EP 683170	B1	19990922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5567820	A	19961022	US 1995-404701	19950315
US 6723739	B1	20040420	US 1995-405555	19950315
CA 2149501	A1	19951121	CA 1995-2149501	19950516
ZA 9503975	A	19961118	ZA 1995-3975	19950516
AT 184880	T	19991015	AT 1995-303265	19950516
ES 2136799	T3	19991201	ES 1995-303265	19950516
AU 9520121	A	19951130	AU 1995-20121	19950517
AU 683734	B2	19971120		
JP 07316180	A	19951205	JP 1995-118338	19950517
FI 9502420	A	19951121	FI 1995-2420	19950518
NO 9501954	A	19951121	NO 1995-1954	19950518
NO 304686	B1	19990201		
CN 1116626	A	19960214	CN 1995-106322	19950518
CN 1039013	B	19980708		
BR 9502079	A	19960305	BR 1995-2079	19950518
HU 73788	A2	19960930	HU 1995-1466	19950518
HU 219335	B	20010328		
IL 113780	A	19990620	IL 1995-113780	19950518
GR 3032142	T3	20000427	GR 1999-403228	19991215
US 2004167080	A1	20040826	US 2004-778865	20040212
PRIORITY APPLN. INFO.:			US 1994-246655 A	19940520
			US 1995-405555 A1	19950315

OTHER SOURCE(S): CASREACT 124:202950
GI



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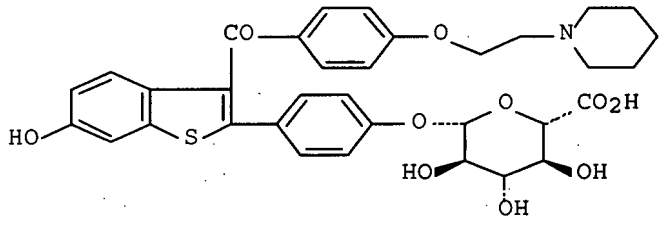


II

AB Raloxifene metabolites (I) and (II) and their hydrochloride salts were prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene

and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-O-tetraacetyl-D-glucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

L3 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:123714 CAPLUS Full-text
DOCUMENT NUMBER: 124:155994
TITLE: Pharmaceutical compositions containing 2-phenyl-3-aryoylbenzothiophenes for for inhibiting bone loss and lowering serum cholesterol
INVENTOR(S): Draper, Michael W.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Can. Pat. Appl., 31 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2141999	A1	19950903	CA 1995-2141999	19950207
US 5478847	A	19951226	US 1994-205012	19940302
ZA 9500976	A	19960807	ZA 1995-976	19950207
NZ 314699	A	20000728	NZ 1995-314699	19950207
EP 674903	A1	19951004	EP 1995-300842	19950210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9500774	A	19950904	NO 1995-774	19950228
RU 2100024	C1	19971227	RU 1995-102778	19950228
RU 2150275	C1	20000610	RU 1996-119781	19950228
AU 9513551	A	19950907	AU 1995-13551	19950301
AU 702575	B2	19990225		
JP 07267861	A	19951017	JP 1995-41769	19950301
JP 2818384	B2	19981030		
BR 9500784	A	19951024	BR 1995-784	19950301
CN 1119530	A	19960403	CN 1995-100021	19950301
HU 72638	A2	19960528	HU 1995-634	19950301
JP 10291932	A	19981104	JP 1998-107550	19950301
JP 10310525	A	19981124	JP 1998-107549	19950301
US 5610168	A	19970311	US 1995-422289	19950414
US 5641790	A	19970624	US 1995-422417	19950414
US 5747510	A	19980505	US 1997-788984	19970127
US 39050	E1	20060328	US 2003-375274	20030227

PRIORITY APPLN. INFO.:		
US 1994-205012	A	19940302
JP 1995-41769	A3	19950301
US 1995-422417	A1	19950414

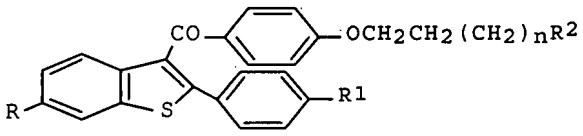
AB A method of inhibiting bone loss or resorption, or lowering serum cholesterol, comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in post-menopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

L3 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:991025 CAPLUS Full-text
DOCUMENT NUMBER: 124:106673
TITLE: Methods for lowering serum cholesterol

INVENTOR(S): Black, Larry J.; Bryant, Henry U.; Cullinan, George J.; Kauffman, Raymond F.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5464845	A	19951107	US 1993-159159	19931130
TW 383306	B	20000301	TW 1993-82100751	19930204
RU 2123335	C1	19981220	RU 1993-55026	19931213
ZA 9309427	A	19950615	ZA 1993-9427	19931215
SK 279271	B6	19980805	SK 1993-1421	19931215
IL 108042	A	19980104	IL 1993-108042	19931216
CZ 283863	B6	19980617	CZ 1993-2790	19931216
HU 69686	A2	19950928	HU 1993-3676	19931220
HU 223342	B1	20040628		
RO 113806	B1	19981130	RO 1993-1739	19931220
PL 177349	B1	19991029	PL 1993-301579	19931220
CA 2112017	A1	19940623	CA 1993-2112017	19931221
CA 2112017	C	20050614		
NO 9304740	A	19940623	NO 1993-4740	19931221
AU 9352578	A	19940707	AU 1993-52578	19931221
AU 669235	B2	19960530		
BR 9305182	A	19940816	BR 1993-5182	19931221
JP 06234632	A	19940823	JP 1993-323825	19931222
JP 3197129	B2	20010813		
CN 1094042	A	19941026	CN 1993-121277	19931222
CN 1043608	B	19990616		
AT 233559	T	20030315	AT 1993-310438	19931222
ES 2193142	T3	20031101	ES 1993-310438	19931222

PRIORITY APPLN. INFO.: US 1992-995222 B2 19921222
OTHER SOURCE(S): MARPAT 124:106673
GI



I

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof. The tested compds. lowered LDL without significantly affecting primary sex targets.

L3 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:362913 CAPLUS Full-text
DOCUMENT NUMBER: 122:213884
TITLE: A chemical probe for the estrogen receptor: synthesis of the 3H-isotopomer of raloxifene
AUTHOR(S): Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C. David
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (1995), 36(1), 43-9
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate was accessed by regioselective aroylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1-piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me ethers in the presence of the ethoxy side-chain followed by palladium catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

L3 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:700754 CAPLUS Full-text
DOCUMENT NUMBER: 121:300754
TITLE: [[(Alkylsulfonyl)oxy]benzo[b]thienyl]methanones and [[(aminocarbonyl)oxy]benzo[b]thienyl]methanones pharmaceuticals
INVENTOR(S): Black, Larry John; Bryant, Henry Uhlman; Cullinan, George Joseph
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 617030	A1	19940928	EP 1994-301871	19940316
EP 617030	B1	19990526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5482949	A	19960109	US 1993-35121	19930319
ZA 9401786	A	19950914	ZA 1994-1786	19940314
CA 2119091	A1	19940920	CA 1994-2119091	19940315
NO 9400940	A	19940920	NO 1994-940	19940316
AU 9457863	A	19940922	AU 1994-57863	19940316
AU 670177	B2	19960704		
BR 9401183	A	19941101	BR 1994-1183	19940316
HU 70549	A2	19951030	HU 1994-774	19940316
AT 180479	T	19990615	AT 1994-301871	19940316
ES 2132339	T3	19990816	ES 1994-301871	19940316
FI 9401262	A	19940920	FI 1994-1262	19940317
JP 06321937	A	19941122	JP 1994-47091	19940317

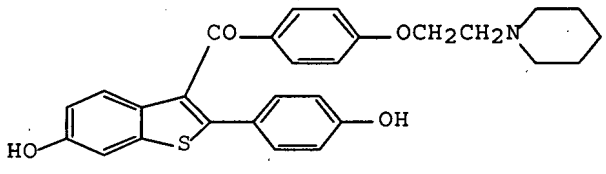
CN 1097420	A	19950118	CN 1994-102910		19940317
US 5994371	A	19991130	US 1995-392445		19950222
US 5599833	A	19970204	US 1996-588670		19960117
US 5605924	A	19970225	US 1996-588663		19960117
US 5798351	A	19980825	US 1997-958535		19971027
PRIORITY APPLN. INFO.:			US 1993-35121	A	19930319
			US 1995-392445	A3	19950222

OTHER SOURCE(S): MARPAT 121:300754
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The (4-alkoxybenzoyl)benzo[b]thiophene-6-sulfonates and (4-alkoxybenzoyl)benzo[b]thien-6-yl carbamates I (R = OH, alkoxysulfonyl, carbamoyl; R1 = H, OH, halo, etc.; R2 = pyrrolidino, piperidino, etc.; X = bond, methine) were disclosed as agents for inhibiting the loss of bone, lowering serum cholesterol levels and therapeutically treating hormone dependent mammalian breast and uterine carcinoma. A specifically claimed example compound is [6-[(pentylsulfonyl)oxy]-2-[4-[(pentylsulfonyl)oxy]phenyl]benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone (II).

L3 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:448784 CAPLUS Full-text
DOCUMENT NUMBER: 101:48784
TITLE: Antiestrogens. 2. Structure-activity studies in a series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone hydrochloride (LY 156758), a remarkably effective estrogen antagonist with only minimal intrinsic estrogenicity
AUTHOR(S): Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.; Peters, Mary K.; Black, Larry J.; Thompson, Allen R.; Falcone, Julie F.; Clemens, James A.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Medicinal Chemistry (1984), 27(8), 1057-66
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



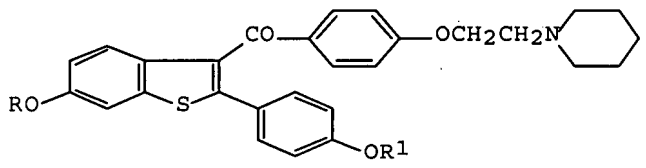
I

AB In an effort to prep. nonsteroidal antiestrogens demonstrating greater antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b]thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino)ethoxy side chain functionality elsewhere in the mol. was AlCl3/EtSH. The benzothiophene derivs. were tested for their ability to inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1- piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. In antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

L3 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:156501 CAPLUS Full-text
DOCUMENT NUMBER: 100:156501
TITLE: Antiestrogenic and antiandrogenic benzothiophenes
INVENTOR(S): Jones, Charles D.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4418068	A	19831129	US 1981-331042	19811216
ZA 8202247	A	19831130	ZA 1982-2247	19820401
PRIORITY APPLN. INFO.:			US 1981-246335 A2	19810403

OTHER SOURCE(S): CASREACT 100:156501
GI



I

AB Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un)substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2-piperidinoethoxy)benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered 0.03 μg estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

L3 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:71917 CAPLUS Full-text
DOCUMENT NUMBER: 98:71917
TITLE: Benzothiophene compounds
INVENTOR(S): Jones, Charles David
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 107 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 62503	A1	19821013	EP 1982-301737		19820401
R: BE, CH, DE, FR, GB, IT, LU, NL, SE					
AU 8282265	A	19821007	AU 1982-82265		19820401
AU 555658	B2	19861002			
GB 2097788	A	19821110	GB 1982-9680		19820401
GB 2097788	B	19850424			
JP 57181081	A	19821108	JP 1982-56479		19820402
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			US 1981-331045	A	19811216

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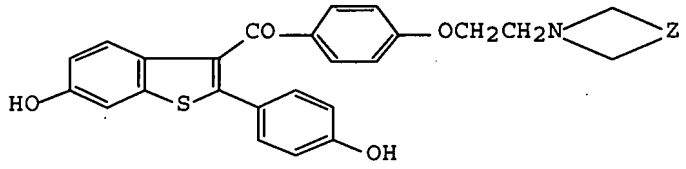

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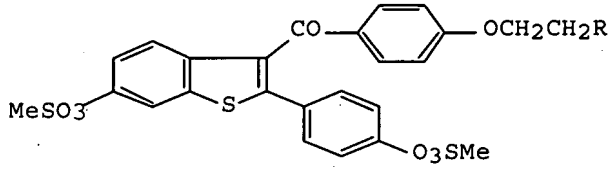


II

AB [(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were prepared, and limited the increase of uterine weight in rats treated with

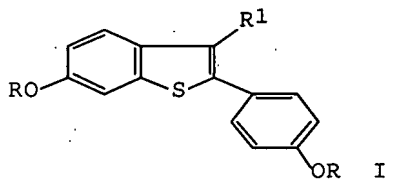
estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).

L3 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:71916 CAPLUS Full-text
DOCUMENT NUMBER: 98:71916
TITLE: 3-(4-Aminoethoxybenzoyl)benzo[b]thiophenes
INVENTOR(S): Jones, Charles David; Goettel, Mary Elizabeth
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62504	A1	19821013	EP 1982-301738	19820401
EP 62504	B1	19860102		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4358593	A	19821109	US 1981-246334	19810403
IL 65378	A	19860228	IL 1982-65378	19820330
CA 1167037	A1	19840508	CA 1982-400300	19820331
GB 2097392	A	19821103	GB 1982-9679	19820401
GB 2097392	B	19850424		
DD 201793	A5	19830810	DD 1982-238654	19820401
CS 227348	B2	19840416	CS 1982-2357	19820401
PL 130867	B1	19840929	PL 1982-235752	19820401
AT 17243	T	19860115	AT 1982-301738	19820401
DK 8201512	A	19821004	DK 1982-1512	19820402
FI 8201160	A	19821004	FI 1982-1160	19820402
JP 57183788	A	19821112	JP 1982-56480	19820402
ES 511124	A1	19830616	ES 1982-511124	19820402
HU 28787	A2	19831228	HU 1982-1026	19820402
HU 191353	B	19870227		
SU 1155157	A3	19850507	SU 1982-3417550	19820402

PRIORITY APPLN. INFO.:
US 1981-246334 A 19810403
US 1981-246335 A 19810403
US 1981-331045 A 19811216
EP 1982-301738 A 19820401

OTHER SOURCE(S): MARPAT 98:71916
GI



I

AB Benzothiophenes I [R = H; R1 = COC6H4O(CH2)2NR2R3-4; R2 = R3 = alkyl; R2R3 = (CH2)4-6, (CH2)2O(CH2)2, etc.] were prepared by Friedel-Crafts acylation of I

(R = Ac, Bz, MeSO2; R1 = H) followed by hydrolysis of the ester groups. Thus, HSC6H4OMe-3 was treated with BrCH2COC6H4OMe-4 to give 3-MeOC6H4SCH2COC6H4OMe-4, which was cyclized with polyphosphoric acid to give I (R = Me, R1 = H). Demethylation of the latter followed by esterification with MeSO2Cl gave I (R = MeSO2, R1 = H; II). Friedel-Crafts acylation of 4 g II with 4-Me2N(CH2)2OC6H4COCl gave 6.2 g I [R = MeSO2, R1 = COC6H4O(CH2)2NMe2-4, III]. Hydrolysis of III gave I (R = H). I are estrogens, antiestrogens, and antiandrogens (no data).

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   115.67     124.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                   -30.42     -30.42

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DICTIONARY FILE UPDATES:  20 AUG 2007  HIGHEST RN 945102-95-4

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on property searching in REGISTRY, refer to:

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=> s e4
L4            1 "RALOXIFENE HYDROCHLORIDE"/CN

=> d l4 1 ide

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   82640-04-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-
     piperidinyl)ethoxy]phenyl]-, hydrochloride (1:1)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-
     piperidinyl)ethoxy]phenyl]-, hydrochloride (9CI)
OTHER NAMES:
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CN Bonebay
CN Bontact
CN Evista
CN Fiona
CN Keoxifene hydrochloride
CN LY 156758
CN Ralofen
CN **Raloxifene hydrochloride**
CN Reloxafine
MF C28 H27 N O4 S . Cl H
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, CSCHEM, EMBASE, HSDB*, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, MSDS-OHS, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
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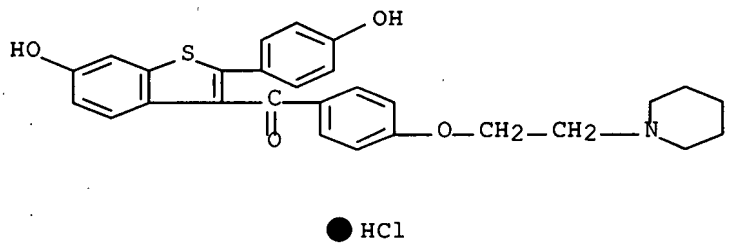
CRN (84449-90-1)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

329 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
329 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.25	132.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-30.42

FILE 'CAPLUS' ENTERED AT 13:35:36 ON 21 AUG 2007

FILE COVERS 1907 - 21 Aug 2007 VOL 147 ISS 9
FILE LAST UPDATED: 20 Aug 2007 (20070820/ED)

=> s l4
L5 329 L4

=> d scan

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 63-6 (Pharmaceuticals)
TI Preparation of raloxifene hydrochloride capsules and establishment of its quality control standard
ST raloxifene hydrochloride capsules dissoln quality control
IT Drug delivery systems
(capsules; preparation of raloxifene hydrochloride capsules and establishment of quality control standard)
IT Dissolution
Quality control
(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)
IT 63-42-3, Lactose 9004-32-4, Carboxymethyl cellulose sodium 9004-34-6, Cellulose, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)
IT **82640-04-8**, Raloxifene hydrochloride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 1
TI Effectiveness of combined GnRH analogue plus raloxifene administration in the treatment of uterine leiomyomas: a prospective, randomized, single-blind, placebo-controlled clinical trial
ST leuprolide acetate SERM raloxifene pelvic pain menorrhagia uterine leiomyomas
IT Human
(GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Intestine, disease
(constipation; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine

leiomyomas)
IT Menopause
(hot flash; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Uterus, neoplasm
(leiomyoma; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Menstrual disorder
(menorrhagia; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Body, anatomical
(pelvis, pain; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Menopause
(premenopause; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective modulator of; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT Urinary system, disease
(urinary frequency; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT 74381-53-6, Leuprolide acetate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Enantone; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)
IT **82640-04-8**, Raloxifene hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC ICM C07D333-64
ICS C07D333-56
CC 27-9 (Heterocyclic Compounds (One Hetero Atom))
TI Demethylation process for preparing benzo[b]thiophenes
ST demethylation benzothiophene benzenethiol
IT 63675-73-0P 63675-74-1P 84541-36-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(demethylation process for preparing benzo[b]thiophenes)
IT 63676-25-5P **82640-04-8P** 84449-87-6P 84449-90-1P
215662-11-6P 215662-12-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(demethylation process for preparing benzo[b]thiophenes)

IT 108-90-7, Chlorobenzene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(demethylation process for preparing benzo[b]thiophenes)
IT 2632-13-5 7340-90-1 7446-70-0, Aluminum chloride, reactions
15570-12-4, 3-Methoxybenzenethiol 84449-80-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(demethylation process for preparing benzo[b]thiophenes)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC ICM A61K031-445
ICS A61K031-40; A61K031-38
INCL 514324000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
TI Methods of decreasing serum calcium levels
ST benzoyl benzothiophene calcium blood decrease; raloxifene calcium blood decrease
IT **82640-04-8**, Raloxifene hydrochloride 84449-90-1, Raloxifene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzoylbenzothiophene derivs. for decreasing serum calcium levels)
IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoylbenzothiophene derivs. for decreasing serum calcium levels)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC C12Q001-02
INCL 435029000
CC 2-1 (Mammalian Hormones)
TI Cell culture for screening estrogen agonists and antagonists
ST estrogen agonist screening cell culture; antagonist estrogen screening cell culture
IT Animal cell line
(C7 MCF7-173, in screening of estrogen agonists/antagonists)
IT Estrogens
RL: ANST (Analytical study)
(agonists, cell culture method for screening of)
IT Cell proliferation
(cells dependent on estrogens for, in screening of estrogen agonists/antagonists)
IT Charcoal
RL: ANST (Analytical study)
(dextran-, human serum stripped with, for maintaining medium in cell culture method for screening of estrogen agonists/antagonists)
IT Blood serum
(fetal bovine, for maintaining medium in cell culture method for screening of estrogen agonists/antagonists)
IT Animal tissue culture
(for estrogen agonist/antagonist screening)
IT Proteins, biological studies
RL: BIOL (Biological study)
(inhibitory to proliferation of estrogen-dependent cells in vitro, for cell culture method for screeing of estrogen agonists/antagonists)
IT Estrogens

RL: PRP (Properties)
(antiestrogens, cell culture method for screening of)
IT Mammary gland
(neoplasm, cells of, in screening of estrogen agonists/antagonists)
IT 50-27-1, Estriol 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies
RL: ANST (Analytical study)
(agonists and antagonists of, cell culture method for screening of)
IT 9004-54-0, Dextran, biological studies
RL: BIOL (Biological study)
(charcoal-, human serum stripped with, for maintaining medium in cell culture method for screening of estrogen agonists/antagonists)
IT 10540-29-1, Tamoxifen 34816-55-2, Moxestrol 63676-25-5, LY117018 71794-60-0, 11β-Chloromethylestradiol **82640-04-8**, LY156758 120382-04-9, RU39411 57-83-0, Progesterone, biological studies
RL: ANST (Analytical study)
(estrogen agonist/antagonist activity of, determination of, cell culture method
for)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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329 L4
4449106 PREP/RL
L6 34 L4/PREP
(L4 (L) PREP/RL)

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YOU HAVE REQUESTED DATA FROM 34 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:265820 CAPLUS Full-text
DOCUMENT NUMBER: 146:448285
TITLE: Benzothiophenes, formulations containing same, and methods
INVENTOR(S): Cullinan, George J.; Palkowitz, Alan D.
PATENT ASSIGNEE(S): USA
SOURCE: Hung. Pat. Appl., 40pp.
CODEN: HUXXCV
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 9901882	A2	20000228	HU 1999-1882	19970219
HU 9901882	A3	20000328		

PRIORITY APPLN. INFO.: HU 1999-1882 19970219
OTHER SOURCE(S): MARPAT 146:448285
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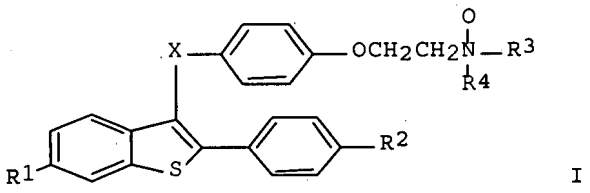


I

AB Benzothiophene N-oxides I [R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, Cl or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-[2-(1- piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.

L6 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:958171 CAPLUS Full-text
DOCUMENT NUMBER: 147:9760
TITLE: Synthesis of raloxifene hydrochloride
AUTHOR(S): Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong, Ping
CORPORATE SOURCE: Shenyang Institute of Chemical Technology, Faculty of Pharmaceutical-Engineering, Shenyang, 110142, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2005), 14(7), 882-884
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3-methoxybenzenethiol and 4-methoxy-α-bromo acetophenone via five steps, including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

L6 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1257978 CAPLUS Full-text
DOCUMENT NUMBER: 144:135192
TITLE: Manufacture of raloxifene-hydrochloride-containing medicines for treating bone fracture delayed union or nonunion
INVENTOR(S): Zhang, Jianhao; Huang, Haibo
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.

CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1615860	A	20050518	CN 2003-10113253	20031111

PRIORITY APPLN. INFO.: CN 2003-10113253 20031111

AB The title medicines are manufd. from (by wt.) raloxifene hydrochloride (35-45%) as effective components, diluent (50-60%), disintegrant (2-4%), lubricant (0.5-1%), and adhesive (2-3%). The medicines can be produced into various drug forms such as tablets, capsules, suspensions, powders, granules, solns., etc., and have advantages of short course of treatment, high recovery rate, etc.

L6 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:547361 CAPLUS Full-text
DOCUMENT NUMBER: 143:59836
TITLE: A process for preparing benzoic acid derivatives, useful as intermediates for preparation of raloxifene
INVENTOR(S): Luke, Wayne Douglas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005137396	A1	20050623	US 2003-745188	20031222
US 7012153	B2	20060314		

PRIORITY APPLN. INFO.: US 2003-745188 20031222
OTHER SOURCE(S): CASREACT 143:59836; MARPAT 143:59836

AB The invention relates to a prepn. of benzoic acid derivs. of formula RO2C-p-C6H4-O(CH2)2-3N(R1)R2 [wherein: R is alkyl; R1 and R2 are independently alkyl, or combined together with the nitrogen atom form piperidinyl, pyrrolidinyl, or morpholinyl, etc.], useful as intermediates for preparation of raloxifene. For instance, 4-[2-(piperidin-1- yl)ethoxy]benzoic acid hydrochloride was prepared via etherification of Me 4-hydroxybenzoate by 1-(β-chloroethyl)piperidine hydrochloride and subsequet hydrolysis with a yield of 99.2%.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:29327 CAPLUS Full-text
DOCUMENT NUMBER: 142:134465
TITLE: Process for preparing raloxifene hydrochloride
INVENTOR(S): Ferrari, Massimo; Zinetti, Fabrizio; Belotti, Paolo
PATENT ASSIGNEE(S): Erregierre S.p.A., Italy
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003116	A1	20050113	WO 2004-EP51263	20040628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2549354	A1	20050113	CA 2004-2549354	20040628
EP 1641773	A1	20060405	EP 2004-741907	20040628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007100147	A1	20070503	US 2005-562762	20051227
PRIORITY APPLN. INFO.:			IT 2003-MI1333 A	20030630
			WO 2004-EP51263 W	20040628

OTHER SOURCE(S): CASREACT 142:134465

AB A process for prepg. raloxifene hydrochloride with a purity greater than 98% and low aluminum content comprises the following stages : (a) demethylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene in pyridine and hydrochloric acid to obtain 6-hydroxy-2-(4- hydroxyphenyl)benzo[b]thiophene in pyridine hydrochloride, (b) acetylation of 6-hydroxy-2-(4-hydroxyphonyl)benzo[b]thiophene with an acetylating agent to obtain the corresponding 6-acetoxy-2-(4- acetoxyphenyl)benzo[b]thiophene (I), (c) acylation of 6-acetoxy-2-(4- acetoxyphonyl)benzo[b]thiophene with 4-(2-piperidinoethoxy)benzoylchloride hydrochloride with aluminum trichloride in a halogenated solvent to obtain 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]- benzo[b]thiophene, (d) hydrolysis of 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2- piperidinoethoxy)benzoyl]benzo[b]thiophene according to the following operating conditions: (d1) treatment of 6-acetoxy-2-(4-acetoxyphonyl)-3-[4- (2-piperidinoethoxy)benzoyl]benzo[b]thiophene with alkaline hydroxide in alc. solvent, (d2) acidification of the product obtained in the preceding stage (d1) with a strong acid, to obtain the corresponding raloxifene salt with the strong acid, characterized in that the strong acid used in stage (d2) is concentrated hydrochloric acid. Thus, thionyl chloride was added to a mixture of 4-(2-piperidinoethoxy)benzoic acid HCl salt and pyridine in refluxing methylene chloride; the mixture was stirred for 1 h and the solvent was distilled off; the mixture was cooled to 20°C, and I was added. The resulting mixture was mixed with aluminum trichloride in methylene chloride at 15°C to 30°C; the mixture was stirred for 1 h and was worked up : the product was treated with sodium hydroxide in methanol; water, Et acetate, and HCl were added; the suspension was centrifuged to give crude raloxifene hydrochloride.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:617920 CAPLUS Full-text

DOCUMENT NUMBER: 142:463529

TITLE: Synthesis of raloxifene hydrochloride

AUTHOR(S): Gong, Ping; Zhao, Yanfang; Wang, Dun

CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop.

Rep. China
SOURCE: Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113
CODEN: SYDXFF; ISSN: 1006-2858
PUBLISHER: Shenyang Yaoke Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 142:463529

AB Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4-hydroxyphenyl)benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3, saponification with 5M NaOH solution in methanol, and saltification with HCl. The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR, 13C NMR.

L6 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:348716 CAPLUS Full-text
DOCUMENT NUMBER: 138:137104
TITLE: Synthesis of Raloxifene hydrochloride as selective estrogen receptor modulator
AUTHOR(S): Chen, Yanzhong; Liu, Yingxiang
CORPORATE SOURCE: Guangdong College of Pharmacy, Canton, 510224, Peop. Rep. China
SOURCE: Guangdong Yaoxueyuan Xuebao (2002), 18(1), 1-3, 20
CODEN: GYXUF8
PUBLISHER: Guangdong Yaoxueyuan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 138:137104

AB Raloxifene was synthesized from α-bromo-p-methoxyacetophenone and m-methoxybenzenethiol via condensation, cyclization, acylation, and demethylation with the overall yield 49.2%. The chemical structure of compound was confirmed by 1H NMR, MS, IR, and elementary anal. The reaction conditions were mild and starting materials were com. available.

L6 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:247325 CAPLUS Full-text
DOCUMENT NUMBER: 134:266100
TITLE: Synthesis of 4-[(2-piperidin-1-yl)ethoxy]benzoic acid for manufacture of Raloxifene hydrochloride
INVENTOR(S): Luke, Wayne Douglas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023369	A2	20010405	WO 2000-US21974	20000918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1220847	A2	20020710	EP 2000-966691		20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003510313	T	20030318	JP 2001-526522		20000918
PRIORITY APPLN. INFO.:			US 1999-156205P	P	19990927
			WO 2000-US21974	W	20000918

OTHER SOURCE(S): CASREACT 134:266100; MARPAT 134:266100

AB An improved process for the prepn. of 4[(2-piperidin-1-yl)ethoxy]benzoic acid derivs. comprises reacting haloalkyl amine X(CH2)nNR1R2 (X = halogen; R1, R2 = C1-4 alkyl, combined with nitrogen atom to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, 1-hexamethyleneimino group; n = 2, 3) with C1-6 alkyl p-hydroxybenzoate in the presence of a hydrated inorg. base in an appropriate solvent.

L6 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:12339 CAPLUS Full-text
DOCUMENT NUMBER: 130:66385
TITLE: Process for preparing benzoic acid derivatives as intermediates in the synthesis of benzothiophenes
INVENTOR(S): Chelius, Erik Christopher
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5852193	A	19981222	US 1998-69277		19980429
US 6075146	A	20000613	US 1998-123889		19980728
PRIORITY APPLN. INFO.:			US 1997-45162P	P	19970430
			US 1998-69277	A3	19980429

OTHER SOURCE(S): CASREACT 130:66385; MARPAT 130:66385
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; R6 = carboxy protecting group] were prepared by reacting a hydroxylamine HO(CH2)nNR1R2 with a compound selected from W2O and W-halo (wherein W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.) followed by reaction of the resulting Y1(CH2)nNR1R2 (Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, etc.) with a compound II. Compds. I can be then reacted with benzothiophenes III (R4, R5 = hydroxy protecting groups) to afford compds. IV (R4, R5 = , H, hydroxy protecting groups) (example of such reaction was given).

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:721690 CAPLUS Full-text
DOCUMENT NUMBER: 130:3769
TITLE: Processes for preparing benzothiophenes
INVENTOR(S): McGill, John McNeil, III; Misner, Jerry Wayne; Zhang, Tony Yantao
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849156	A1	19981105	WO 1998-US8509	19980428
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2287943	A1	19981105	CA 1998-2287943	19980428
AU 9872613	A	19981124	AU 1998-72613	19980428
BR 9809439	A	20000613	BR 1998-9439	19980428
HU 200003187	A2	20010528	HU 2000-3187	19980428
JP 2001522372	T	20011113	JP 1998-547277	19980428
US 6090949	A	20000718	US 1998-69497	19980429
EP 875510	A1	19981104	EP 1998-303374	19980430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
MX 9909883	A	20000331	MX 1999-9883	19991027
PRIORITY APPLN. INFO.:			US 1997-45177P P	19970430
			WO 1998-US8509 W	19980428

OTHER SOURCE(S): CASREACT 130:3769; MARPAT 130:3769
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

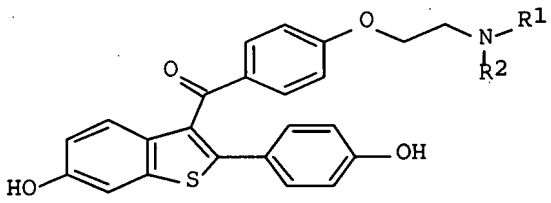
AB The title compds. [I; Y = Cl, Br, I, SO2(C1-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = C1-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:721501 CAPLUS Full-text
DOCUMENT NUMBER: 130:3768
TITLE: Demethylation process for preparing benzo[b]thiophenes
INVENTOR(S): Hoard, David Warren; Luke, Wayne Douglas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 875511	A1	19981104	EP 1998-303345	19980429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2236254	A1	19981030	CA 1998-2236254	19980427
JP 11005789	A	19990112	JP 1998-118628	19980428
US 5994547	A	19991130	US 1998-69500	19980429

PRIORITY APPLN. INFO.: US 1997-45156P P 19970430
OTHER SOURCE(S): CASREACT 130:3768; MARPAT 130:3768
GI



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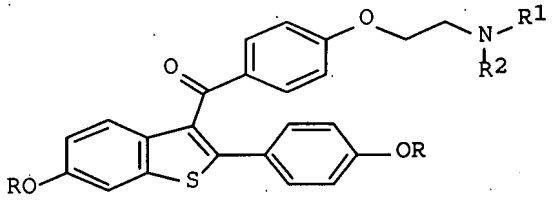


II

AB The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2-methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be carried out in the same reaction vessel without isolation of the acylated, protected material.

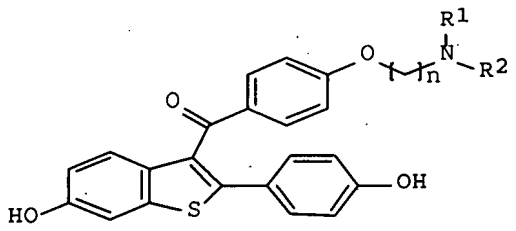
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:721498 CAPLUS Full-text
DOCUMENT NUMBER: 130:3767
TITLE: Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceuticals
INVENTOR(S): Chelius, Erik Christopher
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 875507	A1	19981104	EP 1998-303340	19980429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2231013	A1	19981030	CA 1998-2231013	19980304
JP 10316674	A	19981202	JP 1998-116564	19980427

PRIORITY APPLN. INFO.: US 1997-45162P P 19970430
OTHER SOURCE(S): CASREACT 130:3767; MARPAT 130:3767
GI



I

AB The novel intermediates Y1(CH2)nNR1R2 [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, 2,2,2-trifluoroethylsulfonyloxy, trifluoroacetoxy], useful as intermediates in synthesis of benzothiophenes I and their salts, were prepared by reaction a hydroxylamine HO(CH2)nNR1R2 with W2O and W(halo) [W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.].

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:719256 CAPLUS Full-text
DOCUMENT NUMBER: 130:3764
TITLE: A regioselective alkylation process for preparing substituted benzo[b]thiophenes
INVENTOR(S): McGill, John McNeil, III; Miller, Randal Scot
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

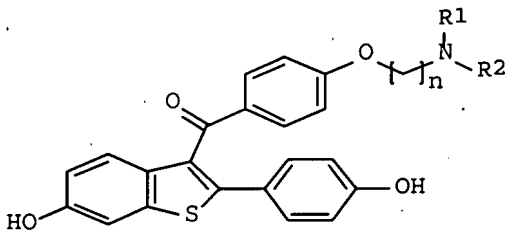
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848792	A1	19981105	WO 1998-US8477	19980428
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,				

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

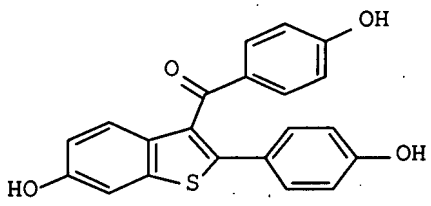
CA 2287918	A1	19981105	CA 1998-2287918	19980428
AU 9871653	A	19981124	AU 1998-71653	19980428
EP 979075	A1	20000216	EP 1998-918798	19980428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2001523252	T	20011120	JP 1998-547259	19980428
US 6025495	A	20000215	US 1998-69276	19980429
PRIORITY APPLN. INFO.:			US 1997-45132P P	19970430
			WO 1998-US8477 W	19980428

OTHER SOURCE(S): CASREACT 130:3764; MARPAT 130:3764

GI



I



II

AB The title benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2, 3] such as raloxifene, were prepared by the regioselective alkylation of benzothiophene II with Y(CH2)nNR1R2 [Y = Cl, p-TsO] in the presence of a suitable base.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:192131 CAPLUS Full-text

DOCUMENT NUMBER: 128:275070

TITLE: Benzothiophenes, formulations containing same, and methods

INVENTOR(S): Cullinan, George Joseph; Palkowitz, Alan David

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 10 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

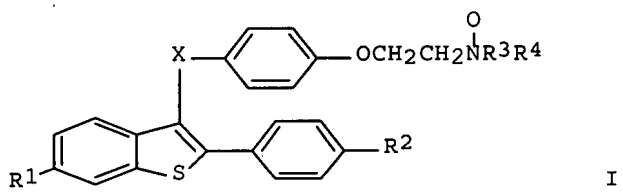
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5731342	A	19980324	US 1997-787041	19970127
PRIORITY APPLN. INFO.:			US 1997-787041	19970127
OTHER SOURCE(S):	MARPAT 128:275070			

GI



I

AB Benzothiophene N-oxides [I; R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, Cl or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-[2-(1- piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1998:161136 CAPLUS Full-text
DOCUMENT NUMBER:	128:221639
TITLE:	Preparation of amorphous benzothiophenes for pharmaceuticals
INVENTOR(S):	Cuff, George W.; Thakkar, Arvind L.
PATENT ASSIGNEE(S):	Eli Lilly and Company, USA; Cuff, George W.; Thakkar, Arvind L.
SOURCE:	PCT Int. Appl., 39 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808513	A1	19980305	WO 1997-US14768	19970822

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN,

ML, MR, NE, SN, TD, TG

EP 826682	A1	19980304	EP 1997-306426		19970822
EP 826682	B1	20030312			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CA 2263175	A1	19980305	CA 1997-2263175		19970822
AU 9742335	A	19980319	AU 1997-42335		19970822
AU 723987	B2	20000907			
IN 182940	A1	19990814	IN 1997-CA1549		19970822
BR 9713176	A	20000208	BR 1997-13176		19970822
CN 1244124	A	20000209	CN 1997-197434		19970822
HU 200001172	A2	20010628	HU 2000-1172		19970822
HU 200001172	A3	20020128			
NZ 333839	A	20010629	NZ 1997-333839		19970822
IL 128641	A	20011031	IL 1997-128641		19970822
TR 9900403	T2	20020121	TR 1999-403		19970822
JP 2002514174	T	20020514	JP 1998-511744		19970822
AT 234295	T	20030315	AT 1997-306426		19970822
ES 2195089	T3	20031201	ES 1997-306426		19970822
ZA 9707617	A	19990225	ZA 1997-7617		19970825
US 6713494	B1	20040330	US 1997-918741		19970825
NO 9900914	A	19990225	NO 1999-914		19990225
KR 2000035941	A	20000626	KR 1999-701682		19990227
PRIORITY APPLN. INFO.:			US 1996-24831P	P	19960828
			WO 1997-US14768	W	19970822

OTHER SOURCE(S): MARPAT 128:221639

AB A method for prepg. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:640660 CAPLUS Full-text

DOCUMENT NUMBER: 127:307297

TITLE: Preparation of 3-[4-(2-aminoethoxy)benzoyl]-2-aryl-6-hydroxybenzo[b]thiophenes.

INVENTOR(S): Jones, Charles David; McGill, John McNeill, III

PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Jones, Charles David; McGill, John McNeill, III

SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734888	A1	19970925	WO 1996-US3934	19960320
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,				

IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2249406	A1	19970925	CA 1996-2249406	19960320
AU 9652586	A	19971010	AU 1996-52586	19960320
EP 888331	A1	19990107	EP 1996-908892	19960320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000506885	T	20000606	JP 1997-533424	19960320
US 6008377	A	19991228	US 1998-125848	19980821
PRIORITY APPLN. INFO.:			US 1996-13674P P	19960319
			WO 1996-US3934 W	19960320

OTHER SOURCE(S): CASREACT 127:307297; MARPAT 127:307297

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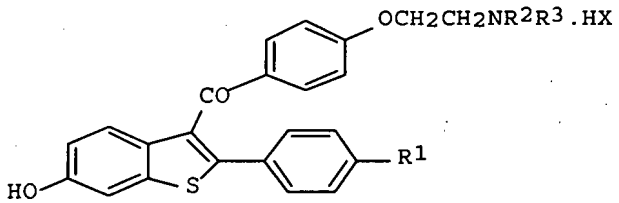

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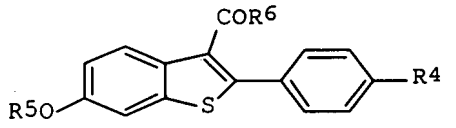

II

AB Title compds. (I; R1 = H, OH; R2, R3 = alkyl; R2R3N = pyrrolidino, piperidino, hexamethyleneimino, morpholino; HX = HCl, HBr) were prepared by reaction of PhOCH2CH2NR2R3.HX (variables as above) with acyl derivative (II; R4 = H, alkoxy; R5 = alkyl; R6 = Cl, Br, OH) in the presence of BX3. Thus, 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene-3-carbonyl chloride (preparation given), and Ph 2-N-piperidinylethyl ether hydrochloride (preparation given) in 1,2-dichloroethane at 0° were treated with BCl3 in 1,2-dichloroethane at 0° followed by warming to 35° for 16-20 h to give 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2- piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride 1,2-dichloroethane solvate.

L6 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1997:124441 CAPLUS Full-text
DOCUMENT NUMBER:	126:143973
TITLE:	Diaryl vinyl sulfoxides, a process for their synthesis, and their use in the preparation of benzothiophene derivatives
INVENTOR(S):	Aikins, James A.; Miller, Randal S.; Zhang, Tony Y.
PATENT ASSIGNEE(S):	Eli Lilly and Co., USA; Aikins, James A.; Miller, Randal S.; Zhang, Tony Y.
SOURCE:	PCT Int. Appl., 45 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9640691	A1	19961219	WO 1996-US9163	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
US 5659087	A	19970819	US 1995-478706	19950607
US 6372945	B1	20020416	US 1995-483130	19950607
CA 2220145	A1	19961219	CA 1996-2220145	19960604
AU 9660920	A	19961230	AU 1996-60920	19960604
AU 697352	B2	19981001		
EP 830361	A1	19980325	EP 1996-918211	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192741	A	19980909	CN 1996-196167	19960604
BR 9608579	A	19990105	BR 1996-8579	19960604
JP 11507061	T	19990622	JP 1996-501552	19960604
HU 9900922	A2	19990728	HU 1999-922	19960604
HU 9900922	A3	20000628		
NZ 337030	A	20001124	NZ 1996-337030	19960604
NZ 337031	A	20010126	NZ 1996-337031	19960604
SG 106558	A1	20041029	SG 1998-4999	19960604
NO 9705578	A	19971203	NO 1997-5578	19971203
NO 5987	A	19971203	NO 2000-5987	20001127
CN 1341596	A	20020327	CN 2000-130779	20001215

PRIORITY APPLN. INFO.:

US 1995-478706	A	19950607
US 1995-483130	A	19950607
NZ 1996-310179	A1	19960604
WO 1996-US9163	W	19960604

OTHER SOURCE(S): CASREACT 126:143973; MARPAT 126:143973

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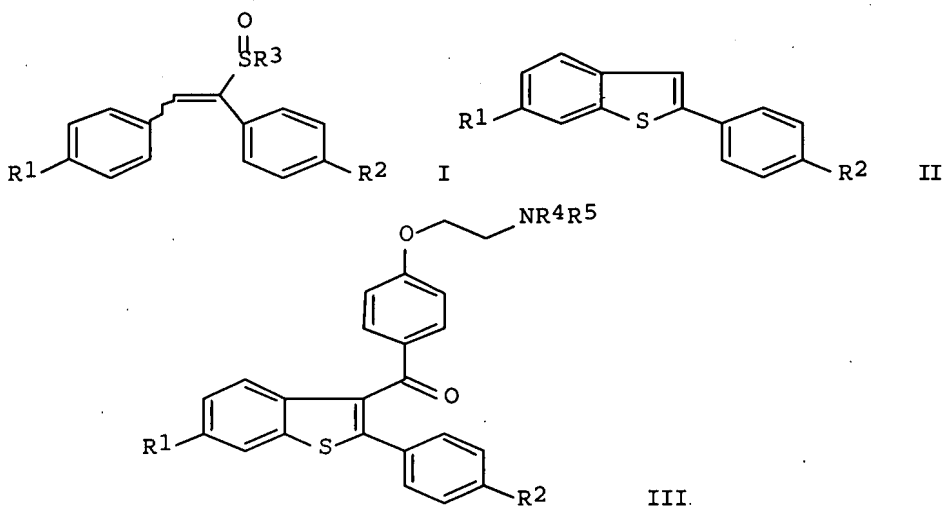

AB The invention is directed to new diarylvinyl sulfoxides I [R1, R2 = H, alkoxy, arylalkoxy, halo, amino; R3 = thermally labile or acid-labile alkyl, alkenyl,

or arylalkyl group], and to a new process for their synthesis. I are useful precursors for 2-aryl-substituted benzothiophenes II, which are in turn intermediates for the drugs III.HX [R1, R2 = H, halo, amino, OH; R4, R5 = alkyl; or NR4R5 = pyrrolidino, piperidino, hexamethyleneimino, morpholino; X = Cl, Br]. For instance, treatment of 4-MeOC6H4CH2COC6H4OMe-4 with TiCl4 in THF and reaction with Me3CSH and Et3N gave the vinyl sulfide (E)-4-MeOC6H4CH:C(SCMe3)C6H4OMe-4 [(E)-IV]. Alternatively, lithiation of 4-MeOC6H4CH2SCMe3 with BuLi and condensation with 4-MeOC6H4CHO gave (Z)-IV. Oxidation of either isomer of IV with a dilute AcOH solution of peracetic acid, in PhMe at -20°, gave the corresponding sulfoxide I [R1 = R2 = OMe; R3 = CMe3]. Dehydrative cyclization of, e.g., the (E)-sulfoxide, using p-MeC6H4SO3H catalyst under Dean-Stark conditions in PhMe, gave the benzothiophene II [R1 = R2 = OMe]. This was acylated by 4-(2-piperidinoethoxy)benzoyl chloride HCl in the presence of BCl3 with concomitant demethylation to give the objective compound III.HCl [R1 = R2 = OH, NR4R5 = piperidino].

L6 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:113406 CAPLUS Full-text
DOCUMENT NUMBER: 126:117861
TITLE: Process for the synthesis of benzo(b)thiophenes
INVENTOR(S): Aikins, James A.; Zhang, Tony Y.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Aikins, James A.; Zhang, Tony Y.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640676	A1	19961219	WO 1996-US9167	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5606076	A	19970225	US 1995-484536	19950607
CA 2223096	A1	19961219	CA 1996-2223096	19960604
AU 9660921	A	19961230	AU 1996-60921	19960604
AU 702928	B2	19990311		
EP 859770	A1	19980826	EP 1996-918212	19960604
EP 859770	B1	19991208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192211	A	19980902	CN 1996-195943	19960604
CN 1086699	B	20020626		
BR 9609062	A	19990126	BR 1996-9062	19960604
JP 11506789	T	19990615	JP 1997-501555	19960604
HU 9900912	A2	19990728	HU 1999-912	19960604
HU 9900912	A3	20000328		
HU 219735	B	20010730		
AT 187450	T	19991215	AT 1996-918212	19960604
ES 2140859	T3	20000301	ES 1996-918212	19960604
PT 859770	T	20000531	PT 1996-918212	19960604
IL 131440	A	20001031	IL 1996-131440	19960604

IL 122378	A	20010319	IL 1996-122378		19960604
NO 9705582	A	19971203	NO 1997-5582		19971203
GR 3032666	T3	20000630	GR 2000-400364		20000214
PRIORITY APPLN. INFO.:			US 1995-484536	A	19950607
			IL 1996-122378	A3	19960604
			WO 1996-US9167	W	19960604

OTHER SOURCE(S): CASREACT 126:117861; MARPAT 126:117861

AB The present invention is directed to a process for the synthesis of 2-arylbenzo[b]thiophenes. E.g., 6-methoxy-2-(4- methoxyphenyl)benzo[b]thiophene was prepared from desoxyanisoin and 2-methyl-2-propanethiol via tert-Bu 4,4'-dimethoxystilbenyl sulfoxide.

L6 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:649600 CAPLUS Full-text

DOCUMENT NUMBER: 125:266032

TITLE: Phosphorous-containing benzothiophenes, their preparation, their use in treating postmenopausal syndrome-associated indications and estrogen-dependent diseases, and pharmaceuticals containing them

INVENTOR(S): Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey S.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 729964	A1	19960904	EP 1996-300878	19960209
EP 729964	B1	20010509		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 6479517	B1	20021112	US 1995-395944	19950228
ES 2158242	T3	20010901	ES 1996-300878	19960209
CA 2169414	A1	19960829	CA 1996-2169414	19960213
JP 08259560	A	19961008	JP 1996-25281	19960213
US 5998443	A	19991207	US 1997-946842	19971008
PRIORITY APPLN. INFO.:			US 1995-395944	A 19950228

OTHER SOURCE(S): MARPAT 125:266032

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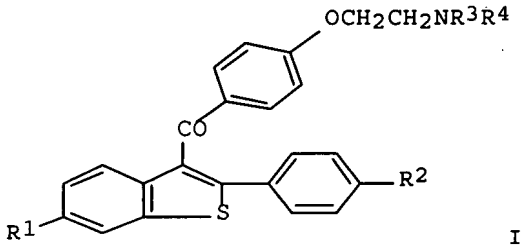


I

AB Phosphorus-contg. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(O-alkyl)2, OPO(O-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3-dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds. of the invention, as well as pharmaceutical compns. containing compds. of the invention.

L6 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:319150 CAPLUS Full-text
DOCUMENT NUMBER: 125:86484
TITLE: Preparation of vinyl sulfenic acid derivatives as benzo[b]thiophene intermediates
INVENTOR(S): Hoard, David W.; Luke, Wayne D.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5512701	A	19960430	US 1995-482692	19950607
CA 2224225	A1	19961219	CA 1996-2224225	19960604
WO 9640693	A1	19961219	WO 1996-US9460	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
AU 9661003	A	19961230	AU 1996-61003	19960604
AU 698076	B2	19981022		
EP 830362	A1	19980325	EP 1996-918314	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1192215	A	19980902	CN 1996-195947	19960604
CN 1068883	B	20010725		
BR 9608847	A	19990608	BR 1996-8847	19960604
JP 11507346	T	19990629	JP 1997-501774	19960604
HU 9900923	A2	19990728	HU 1999-923	19960604
HU 9900923	A3	20000228		
IL 122127	A	20010520	IL 1996-122127	19960604
NO 9705633	A	19980128	NO 1997-5633	19971204
CN 1330071	A	20020109	CN 2000-130796	20001212
PRIORITY APPLN. INFO.:			US 1995-482692 A	19950607
			US 1995-483607 A	19950607
			WO 1996-US9460 W	19960604

OTHER SOURCE(S): CASREACT 125:86484; MARPAT 125:86484
AB 4-R1C6H4CH:C(R9)C6H4R2-4 [I; R1,R2 = H, (ar)alkoxy, halo, NH2; R9 = SR4; R4 = OSi(R)3, NR5R6, SR8; R = (ar)alkyl, aryl; R5,R6 = H, (ar)alkyl; NR5R6 =

pyrrolidino, piperidino, etc.; R8 = (ar)alkyl, aryl] were prepared by treating I [R9 = SOR3; R3 = labile alk(en)yl or aryl] with a silylating agent optionally followed by reaction with HNR5R6 or HSR8. Thus, (E)-I (R1 = R2 = OMe)(II; R9 = SOCMe3)(preparation given) was treated with (Me2CSiNH)2CO in PhMe followed by Me2NH, in the same pot, to give I (R1 = R2 = OMe, R9 = SNMe2) as a mixture of (E)- and (Z)-isomers. The latter mixt was treated with TsOH to give 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophe ne.

L6 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:307324 CAPLUS Full-text
DOCUMENT NUMBER: 124:343103
TITLE: Preparation of unsolvated crystalline 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride.
INVENTOR(S): Smith Labell, Elizabeth; Luke, Wayne Douglas; McNeill McGill, John, III; Miller, Randal Scot
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19534744	A1	19960321	DE 1995-19534744	19950919
US 5629425	A	19970513	US 1994-308325	19940919
IN 1995CA00614	A	20050304	IN 1995-CA614	19950530
IN 1995CA00615	A	20050304	IN 1995-CA615	19950530
TW 389760	B	20000511	TW 1995-84105614	19950605
TW 412534	B	20001121	TW 1995-84105613	19950605
US 5731327	A	19980324	US 1995-467485	19950606
EG 21479	A	20011128	EG 1995-455	19950606
US 6399778	B1	20020604	US 1995-469093	19950606
US 6472531	B1	20021029	US 1995-469961	19950606
ES 2109882	A1	19980116	ES 1995-1774	19950913
ES 2109882	B1	19980816		
ES 2129293	A1	19990601	ES 1995-1775	19950913
ES 2129293	B1	20000116		
NL 1001194	A1	19960319	NL 1995-1001194	19950914
NL 1001194	C2	19970404		
NL 1001196	A1	19960319	NL 1995-1001196	19950914
NL 1001196	C2	19970404		
ZA 9507752	A	19970314	ZA 1995-7752	19950914
ZA 9507753	A	19970314	ZA 1995-7753	19950914
IL 115315	A	19990922	IL 1995-115315	19950914
IL 115314	A	20000229	IL 1995-115314	19950914
IL 125283	A	20010614	IL 1995-125283	19950914
IN 1995CA01111	A	20051021	IN 1995-CA1111	19950914
CA 2158399	A1	19960320	CA 1995-2158399	19950915
CA 2158399	C	20010320		
CA 2158400	A1	19960320	CA 1995-2158400	19950915
CA 2158400	C	20061024		
DK 9501027	A	19960320	DK 1995-1027	19950915
DK 175903	B1	20050606		
DK 9501028	A	19960320	DK 1995-1028	19950915
DK 175897	B1	20050530		

NO	9503657	A	19960320	NO 1995-3657	19950915
NO	308107	B1	20000724		
NO	9503658	A	19960320	NO 1995-3658	19950915
NO	313996	B1	20030113		
SE	9503213	A	19960320	SE 1995-3213	19950915
SE	520721	C2	20030812		
SE	9503214	A	19960320	SE 1995-3214	19950915
SE	509265	C2	19981221		
RO	115259	B1	19991230	RO 1995-1619	19950915
RO	115260	B1	19991230	RO 1995-1620	19950915
CZ	290343	B6	20020717	CZ 1995-2403	19950915
CZ	292007	B6	20030716	CZ 1995-2402	19950915
FI	9504402	A	19960320	FI 1995-4402	19950918
FI	112226	B1	20031114		
FI	9504403	A	19960320	FI 1995-4403	19950918
FR	2724655	A1	19960322	FR 1995-10921	19950918
FR	2724655	B1	19971114		
GB	2293382	A	19960327	GB 1995-19028	19950918
GB	2293382	B	19980819		
GB	2293602	A	19960403	GB 1995-19032	19950918
GB	2293602	B	19980506		
AU	9531730	A	19960404	AU 1995-31730	19950918
AU	691955	B2	19980528		
AU	9531731	A	19960404	AU 1995-31731	19950918
AU	692907	B2	19980618		
JP	08176147	A	19960709	JP 1995-238211	19950918
JP	2860071	B2	19990224		
CN	1127253	A	19960724	CN 1995-118629	19950918
CN	1075069	B	20011121		
JP	08193081	A	19960730	JP 1995-238209	19950918
LV	11177	B	19960820	LV 1995-284	19950918
LV	11178	B	19960820	LV 1995-285	19950918
BR	9504059	A	19960924	BR 1995-4059	19950918
BR	9504060	A	19960924	BR 1995-4060	19950918
FR	2732020	A1	19960927	FR 1995-10922	19950918
FR	2732020	B1	19971114		
CN	1132205	A	19961002	CN 1995-118449	19950918
CN	1068324	B	20010711		
HU	74178	A2	19961128	HU 1995-2723	19950918
HU	75033	A2	19970328	HU 1995-2721	19950918
HU	225417	B1	20061128		
BE	1009625	A3	19970603	BE 1995-760	19950918
BE	1009626	A3	19970603	BE 1995-761	19950918
RU	2104278	C1	19980210	RU 1995-116242	19950918
RU	2108331	C1	19980410	RU 1995-116238	19950918
AT	9501542	A	20001215	AT 1995-1542	19950918
CH	691125	A5	20010430	CH 1995-2629	19950918
CH	691431	A5	20010731	CH 2000-2062	19950918
CH	691478	A5	20010731	CH 1995-2628	19950918
CH	691594	A5	20010831	CH 1995-1780	19950918
PL	182450	B1	20020131	PL 1995-310518	19950918
HR	950483	B1	20030228	HR 1995-483	19950918
PL	187686	B1	20040930	PL 1995-310517	19950918
HR	950482	B1	20070430	HR 1995-482	19950918
AT	502957	A1	20070615	AT 1995-1543	19950918
WO	9609045	A1	19960328	WO 1995-US11872	19950919

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

DE 19534745	A1	19960404	DE 1995-19534745	19950919
DE 19534745	B4	20040609		
AU 9537186	A	19960409	AU 1995-37186	19950919
EE 3386	B1	20010416	EE 1997-55	19950919
SK 283502	B6	20030805	SK 1997-233	19950919
DE 19549755	B4	20050504	DE 1995-19549755	19950919
DK 9700027	A	19970109	DK 1997-27	19970109
DK 175887	B1	20050523		
DK 9700028	A	19970109	DK 1997-28	19970109
DK 175886	B1	20050523		
CZ 290344	B6	20020717	CZ 2001-3548	20011002
US 2002173645	A1	20021121	US 2002-83179	20020226
PRIORITY APPLN. INFO.:			US 1994-308325 A	19940919
			US 1995-427914 A	19950426
			US 1995-469093 A1	19950606
			IL 1995-115315 A3	19950914
			CZ 1995-2402 A3	19950915
			DE 1995-19534744 A1	19950919
			WO 1995-US11872 W	19950919

AB Title compd. (I) (raloxifene hydrochloride) having a specified X-ray diffraction pattern, was prepared Thus, 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene (preparation given) and 4-(2-piperidinoethoxy)benzoyl chloride hydrochloride (preparation given) in CH2Cl2 was treated with BCl3 at 0 for 8 h and at 35° for 16 h to give I.1,2-dichloroethane of 86.8% purity. The latter in MeOH was treated with NaOH and activated C followed by filtration, treatment with HCl, and crystallization to give 99.1% pure I.

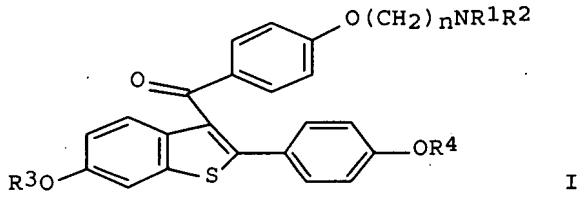
L6 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:256453 CAPLUS Full-text
DOCUMENT NUMBER: 124:289251
TITLE: Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceutical agents
INVENTOR(S): Kjell, Douglas Patton; Perry, Fred Mason
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 699672	A1	19960306	EP 1995-306050	19950830
EP 699672	B1	19980422		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5631369	A	19970520	US 1994-298636	19940831
IL 128881	A	20001206	IL 1995-128881	19950828
CA 2157236	A1	19960301	CA 1995-2157236	19950830
FI 9504067	A	19960301	FI 1995-4067	19950830
HU 73141	A2	19960628	HU 1995-2537	19950830
HU 222121	B1	20030428		
BR 9503846	A	19960917	BR 1995-3846	19950830
AT 165355	T	19980515	AT 1995-306050	19950830
ES 2114721	T3	19980601	ES 1995-306050	19950830

TW 427975	B	20010401	TW 1995-84109069		19950830
JP 08119964	A	19960514	JP 1995-223183		19950831
US 5750688	A	19980512	US 1996-629862		19960409
PRIORITY APPLN. INFO.:			US 1994-298636	A	19940831
			IL 1995-115092	A3	19950828

OTHER SOURCE(S): MARPAT 124:289251
GI



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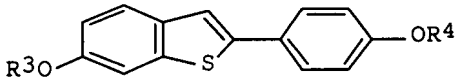

II

AB The present invention provides a novel process for prepg. novel compds. of formula HO2C(p-C6H4)O(CH2)nNR1R2 [R1, R2 = C1-C4 alkyl, combine to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2)nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compds. of formula RO2C(p-C6H4)OH [R = C1-C6 alkyl], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product of step (a) with an aqueous acid; and (c) cleaving the ester of the reaction product from step (b) to form an acid. The present invention further provides a novel process for preparing compds. of Formula I [R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidino, methylpyrrolidino, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; R3, R4 = H, hydroxy protecting group; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2)nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compound of formula RO2C(p-C6H4)OH [R = C1-C6 alky], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product from step (a) with an aqueous acid; (c) cleaving the ester of the reaction product from step (b) to form an acid; (d) reacting the extracted product from step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing R3 and R4 hydroxy protecting groups of the reaction product from step (d); and (f) optionally forming a salt of the reaction from either steps (d) or step (e).

L6 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:150242 CAPLUS Full-text
DOCUMENT NUMBER: 124:202950
TITLE: Preparation of benzothiophene glucopyranosides as antihyperlipidemics.
INVENTOR(S): Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom, Terry Donald; Lugar, Charles Willis Iii; Staten, Gilbert Stanley
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 683170	A1	19951122	EP 1995-303265	19950516
EP 683170	B1	19990922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5567820	A	19961022	US 1995-404701	19950315
US 6723739	B1	20040420	US 1995-405555	19950315
CA 2149501	A1	19951121	CA 1995-2149501	19950516
ZA 9503975	A	19961118	ZA 1995-3975	19950516
AT 184880	T	19991015	AT 1995-303265	19950516
ES 2136799	T3	19991201	ES 1995-303265	19950516
AU 9520121	A	19951130	AU 1995-20121	19950517
AU 683734	B2	19971120		
JP 07316180	A	19951205	JP 1995-118338	19950517
FI 9502420	A	19951121	FI 1995-2420	19950518
NO 9501954	A	19951121	NO 1995-1954	19950518
NO 304686	B1	19990201		
CN 1116626	A	19960214	CN 1995-106322	19950518
CN 1039013	B	19980708		
BR 9502079	A	19960305	BR 1995-2079	19950518
HU 73788	A2	19960930	HU 1995-1466	19950518
HU 219335	B	20010328		
IL 113780	A	19990620	IL 1995-113780	19950518
GR 3032142	T3	20000427	GR 1999-403228	19991215
US 2004167080	A1	20040826	US 2004-778865	20040212
PRIORITY APPLN. INFO.:			US 1994-246655 A	19940520
			US 1995-405555 A1	19950315

OTHER SOURCE(S): CASREACT 124:202950
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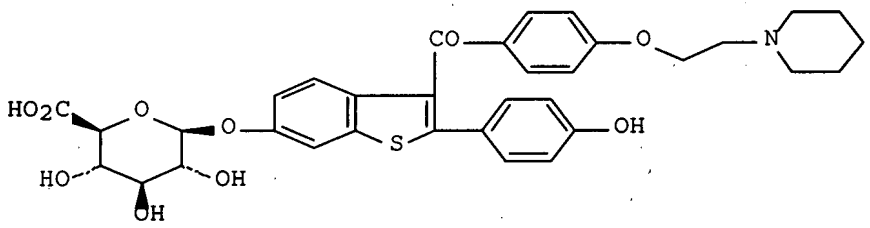

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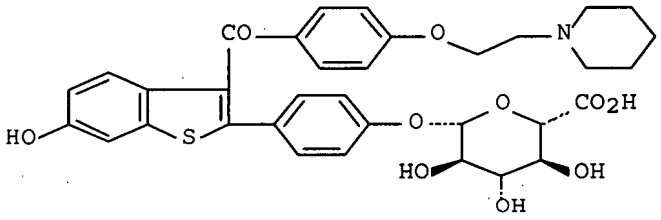

II

AB Raloxifene metabolites (I) and (II) and their hydrochloride salts were prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-O-tetraacetyl-D-glucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

L6 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:123714 CAPLUS Full-text
DOCUMENT NUMBER: 124:155994
TITLE: Pharmaceutical compositions containing 2-phenyl-3-aryoylbenzothiophenes for for inhibiting bone loss and lowering serum cholesterol
INVENTOR(S): Draper, Michael W.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Can. Pat. Appl., 31 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2141999	A1	19950903	CA 1995-2141999	19950207
US 5478847	A	19951226	US 1994-205012	19940302
ZA 9500976	A	19960807	ZA 1995-976	19950207
NZ 314699	A	20000728	NZ 1995-314699	19950207
EP 674903	A1	19951004	EP 1995-300842	19950210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9500774	A	19950904	NO 1995-774	19950228
RU 2100024	C1	19971227	RU 1995-102778	19950228
RU 2150275	C1	20000610	RU 1996-119781	19950228
AU 9513551	A	19950907	AU 1995-13551	19950301
AU 702575	B2	19990225		
JP 07267861	A	19951017	JP 1995-41769	19950301
JP 2818384	B2	19981030		
BR 9500784	A	19951024	BR 1995-784	19950301
CN 1119530	A	19960403	CN 1995-100021	19950301
HU 72638	A2	19960528	HU 1995-634	19950301
JP 10291932	A	19981104	JP 1998-107550	19950301
JP 10310525	A	19981124	JP 1998-107549	19950301
US 5610168	A	19970311	US 1995-422289	19950414
US 5641790	A	19970624	US 1995-422417	19950414
US 5747510	A	19980505	US 1997-788984	19970127
US 39050	E1	20060328	US 2003-375274	20030227
PRIORITY APPLN. INFO.:			US 1994-205012 A	19940302
			JP 1995-41769 A3	19950301
			US 1995-422417 A1	19950414

AB A method of inhibiting bone loss or resorption, or lowering serum cholesterol, comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in post-menopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

L6 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:991025 CAPLUS Full-text

DOCUMENT NUMBER: 124:106673
TITLE: Methods for lowering serum cholesterol
INVENTOR(S): Black, Larry J.; Bryant, Henry U.; Cullinan, George J.; Kauffman, Raymond F.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5464845	A	19951107	US 1993-159159	19931130
TW 383306	B	20000301	TW 1993-82100751	19930204
RU 2123335	C1	19981220	RU 1993-55026	19931213
ZA 9309427	A	19950615	ZA 1993-9427	19931215
SK 279271	B6	19980805	SK 1993-1421	19931215
IL 108042	A	19980104	IL 1993-108042	19931216
CZ 283863	B6	19980617	CZ 1993-2790	19931216
HU 69686	A2	19950928	HU 1993-3676	19931220
HU 223342	B1	20040628		
RO 113806	B1	19981130	RO 1993-1739	19931220
PL 177349	B1	19991029	PL 1993-301579	19931220
CA 2112017	A1	19940623	CA 1993-2112017	19931221
CA 2112017	C	20050614		
NO 9304740	A	19940623	NO 1993-4740	19931221
AU 9352578	A	19940707	AU 1993-52578	19931221
AU 669235	B2	19960530		
BR 9305182	A	19940816	BR 1993-5182	19931221
JP 06234632	A	19940823	JP 1993-323825	19931222
JP 3197129	B2	20010813		
CN 1094042	A	19941026	CN 1993-121277	19931222
CN 1043608	B	19990616		
AT 233559	T	20030315	AT 1993-310438	19931222
ES 2193142	T3	20031101	ES 1993-310438	19931222

PRIORITY APPLN. INFO.: US 1992-995222 B2 19921222
OTHER SOURCE(S): MARPAT 124:106673
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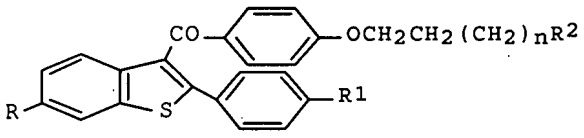

I

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof.

The tested compds. lowered LDL without significantly affecting primary sex targets.

L6 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:934099 CAPLUS Full-text
DOCUMENT NUMBER: 123:339764
TITLE: Processes for preparing 3-(benzoyl)-2-(4-hydroxyphenyl)benzothiophenes
INVENTOR(S): Dodge, Jeffrey Alan; Stocksdale, Mark Gregory
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 675121	A1	19951004	EP 1995-302076	19950328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2145614	A1	19951001	CA 1995-2145614	19950327
JP 07278138	A	19951024	JP 1995-73418	19950330
US 5808061	A	19980915	US 1995-503444	19950717
PRIORITY APPLN. INFO.:			US 1994-220853 A	19940331

OTHER SOURCE(S): CASREACT 123:339764; MARPAT 123:339764
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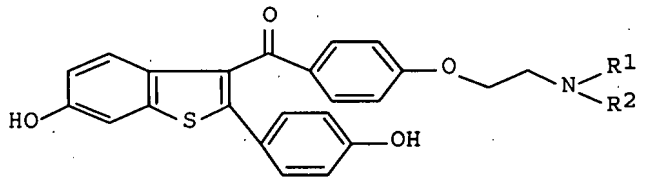

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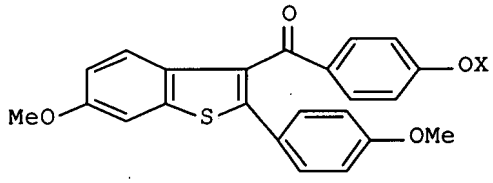

II

AB The title compds. [I; R1R2 = C4-6 polymethylene, CH2CH(CH3)CH2CH2, CH2C(CH3)2CH2CH2, CH2CH2OCH2CH2] [e.g., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride], useful for the treatment of osteoporosis in post-menopausal women (no data), are prepared by: (a) coupling a benzothiophene (II; X = H) with a (hydroxyethyl)amine HOCH2CH2N(R1)R2 in the presence of P(Ph3) and di-Et azodicarboxylate; or (b) reacting a benzothiophene (II; X = CH2CH2Z; Z = leaving group) with pyrrolidine, piperidine, hexamethyleneimine, methylpyrrolidine, dimethylpyrrolidine, or morpholine; (c) deprotecting the 6- and 4-position hydroxy groups of the reaction product of step (a) or step (b);

and (d) optionally salifying or forming a solvate of the reaction product of step (c).

L6 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:661193 CAPLUS Full-text
DOCUMENT NUMBER: 123:111843
TITLE: 2-amino-3-aroylbenzo[b]thiophenes and methods for preparing and using same to produce 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-aminoethoxy)benzoyl]benzo[b]thiophene
INVENTOR(S): Godfrey, Alexander G.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5420349	A	19950530	US 1994-258641	19940610
CA 2192096	A1	19951221	CA 1995-2192096	19950607
WO 9534536	A1	19951221	WO 1995-US7399	19950607
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9528236	A	19960105	AU 1995-28236	19950607
EP 764150	A1	19970326	EP 1995-923804	19950607
EP 764150	B1	19991027		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 76000	A2	19970630	HU 1996-3404	19950607
HU 213834	B	19971028		
HU 76525	A2	19970929	HU 1996-3403	19950607
HU 216272	B	19990528		
BR 9507968	A	19971118	BR 1995-7968	19950607
JP 10503175	T	19980324	JP 1996-502366	19950607
AT 186050	T	19991115	AT 1995-923804	19950607
ES 2139222	T3	20000201	ES 1995-923804	19950607
HU 217822	B	20000428	HU 1998-2648	19950607
FI 9604854	A	19961204	FI 1996-4854	19961204
GR 3032409	T3	20000531	GR 2000-400106	20000119
PRIORITY APPLN. INFO.:			US 1994-258641 A	19940610
			WO 1995-US7399 W	19950607

OTHER SOURCE(S): CASREACT 123:111843; MARPAT 123:111843
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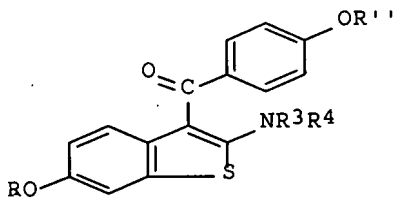

I

AB A group of 2-amino-3-aroyl-benzo[b]thiophenes (I) are prepd. by prepg. an α-hydroxy thioacetamide 4-ROC6H4CH(OH)C(:S)NR9R9 (II) wherein R, R8 and R9 independently represent C1-C6 alkyl; comprising: (a) reacting an alkyl imidate of the formula 4-ROC6H4CH(OH)C(:NH.protic acid)OR''' where R''' is C1-C6 alkyl, with a sulfur compound to yield a thioester of the formula 4-ROC6H4CH(OH)C(:S)OR'''; (b) reacting the thioester with a dialkylamine of the formula HNR8R9 to yield the α-hydroxy thioacetamide; said steps being conducted without isolation or purification of the thioester., cyclizing II, and subsequently acylating the benzo[b]thiophene to yield the 2-amino-3-aryl derivative These compds. may be treated with suitable Ph Grignard reagents, and after deprotection, yield 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thi ophene. %Thus, e.g., p-anisaldehyde was converted to p- methoxybenzaldehyde cyanohydrin (80% yield) and subsequently to the Me imidate 4-MeOC6H4CH(OH)C(:NH.HCl)OMe (85-90% yield); reaction of the latter with H2S/Me2NH afforded α-(4-methoxy phenyl)-α-hydroxy- N,N-dimethylthioacetamide (70%) which was cyclized with methanesulfonic acid to 2-N,N-dimethylamino-6-methoxybenzo[b]thiophene (79%); acylation of the latter with 4-(2-piperidinoethoxy)benzoyl chloride hydrochloride (autocatalytic) afforded 2-N,N-dimethylamino-6-methoxy-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (I; R = Me, R3 = R4 = Me, R'' = 2-piperidinoethyl; 74%) which underwent Grignard reaction with 4-methoxyphenylmagnesium bromide to afford 2-(4-methoxyphenyl)-6- methoxy-3-[4-(piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (90%); deprotection of the latter with AlCl3/propanethiol afforded 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thi ophene hydrochloride (95% yield).

L6 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:362913 CAPLUS Full-text
DOCUMENT NUMBER: 122:213884
TITLE: A chemical probe for the estrogen receptor: synthesis of the 3H-isotopomer of raloxifene
AUTHOR(S): Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C. David
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (1995), 36(1), 43-9
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate was accessed by regioselective aroylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1-piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me ethers in the presence of the ethoxy side-chain followed by palladium

catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

L6 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:433189 CAPLUS Full-text
DOCUMENT NUMBER: 107:33189
TITLE: Treatment of mammary cancer
INVENTOR(S): Black, Larry J.; Clemens, James A.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 10 pp. Cont. of U.S. Ser. No. 289,360, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4656187	A	19870407	US 1983-556875	19831201
PRIORITY APPLN. INFO.:			US 1981-289360 A1	19810803

AB A method of inhibiting the growth of estrogen-dependent mammary cancers comprises administering about 20 mg/kg/day of a 1st compound 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-pyrrolidinoethoxy)benzoyl]benzo[b]th iophene (I) and .apprx.5 mg/kg/day of a 2nd compound tamoxifen (II). Also, a pharmaceutical combination comprises .apprx.4 parts by weight of I and .apprx.1 part by weight of II. I hydrochloride was prepared by reacting 4-(2-pyrrolidinoethoxy)benzoic acid with thionyl chloride and then with 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene (prepared from 3-methoxybenzenethiol and α-bromo-4-methoxyacetophenone). Oral doses of I 20 and II 5 mg/kg/day were given for 8 wks to rats with induced mammary tumors. Half of the rats receiving the combination treatment experienced a total regression of their tumors. The rest had only a very modest growth of their tumors during the treatment. A synergistic effect was shown.

L6 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:448784 CAPLUS Full-text
DOCUMENT NUMBER: 101:48784
TITLE: Antiestrogens. 2. Structure-activity studies in a series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone hydrochloride (LY 156758), a remarkably effective estrogen antagonist with only minimal intrinsic estrogenicity
AUTHOR(S): Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.; Peters, Mary K.; Black, Larry J.; Thompson, Allen R.; Falcone, Julie F.; Clemens, James A.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Medicinal Chemistry (1984), 27(8), 1057-66
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
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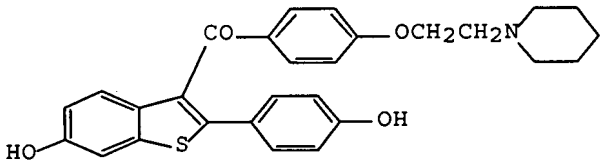

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AB In an effort to prep. nonsteroidal antiestrogens demonstrating greater antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b]thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino)ethoxy side chain functionality elsewhere in the mol. was AlCl3/EtSH. The benzothiophene derivs. were tested for their ability to inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1- piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. In antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

L6 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:156501 CAPLUS Full-text
DOCUMENT NUMBER: 100:156501
TITLE: Antiestrogenic and antiandrogenic benzothiophenes
INVENTOR(S): Jones, Charles D.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4418068	A	19831129	US 1981-331042	19811216
ZA 8202247	A	19831130	ZA 1982-2247	19820401
PRIORITY APPLN. INFO.:			US 1981-246335 A2	19810403

OTHER SOURCE(S): CASREACT 100:156501
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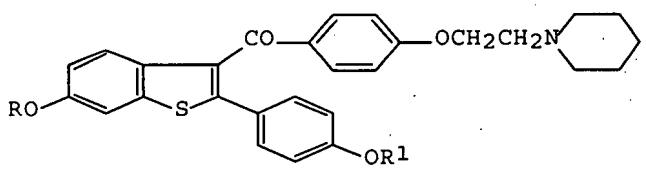

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AB Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un)substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2-piperidinoethoxy)benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered 0.03 μg estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

L6 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:422309 CAPLUS Full-text
DOCUMENT NUMBER: 99:22309
TITLE: Acylated benzothiophenes
INVENTOR(S): Peters, Mary K.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 246,333, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4380635	A	19830419	US 1981-331046	19811216
CA 1167036	A1	19840508	CA 1982-400262	19820331
EP 62505	A1	19821013	EP 1982-301739	19820401
EP 62505	B1	19850724		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
GB 2096608	A	19821020	GB 1982-9681	19820401
GB 2096608	B	19850612		
DD 201794	A5	19830810	DD 1982-238653	19820401
CS 227347	B2	19840416	CS 1982-2356	19820401
RO 84584	A1	19840717	RO 1982-107118	19820401
PL 130584	B1	19840831	PL 1982-235751	19820401
AT 14429	T	19850815	AT 1982-301739	19820401
DK 8201513	A	19821004	DK 1982-1513	19820402
FI 8201161	A	19821004	FI 1982-1161	19820402
JP 57181079	A	19821108	JP 1982-56481	19820402
ES 511123	A1	19830216	ES 1982-511123	19820402
HU 28746	A2	19831228	HU 1982-1025	19820402
HU 191084	B	19870128		
SU 1138028	A3	19850130	SU 1982-3417251	19820402

PRIORITY APPLN. INFO.: US 1981-246333 A2 19810403
US 1981-246335 A 19810403

US 1981-331045	A	19811216
US 1981-331046	A	19811216
EP 1982-301739	A	19820401

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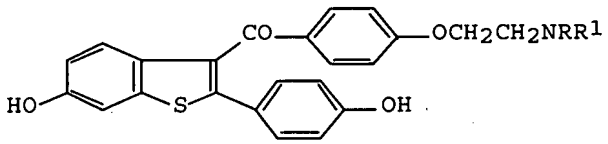

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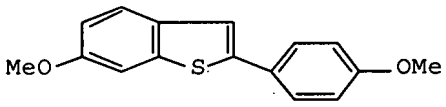

II

AB The acylated benzothiophenones I (R,R1 = C1-4 alkyl, RR1 = polymethylene, CH2CHMeCH2CH2, CH2CH2OCH2CH2) were prepared by acylation-demethylation of benzothiophenes II. Thus, 3-MeOC6H4SN was treated with BrCH2COC6H4OMe-p followed by cyclization to give II, which was treated with AlCl3 and the acid chloride of 4-(2-piperidinoethoxy)benzoic acid to give I (NRR1 = piperidino).

L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:71918 CAPLUS Full-text
DOCUMENT NUMBER: 98:71918
TITLE: Acylated benzothiophenes
INVENTOR(S): Peters, Mary Kathleen; Jones, Charles David
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62505	A1	19821013	EP 1982-301739	19820401
EP 62505	B1	19850724		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4380635	A	19830419	US 1981-331046	19811216
AT 14429	T	19850815	AT 1982-301739	19820401

PRIORITY APPLN. INFO.:	US 1981-246333	A	19810403
	US 1981-246335	A	19810403
	US 1981-331045	A	19811216
	US 1981-331046	A	19811216
	EP 1982-301739	A	19820401

OTHER SOURCE(S): MARPAT 98:71918
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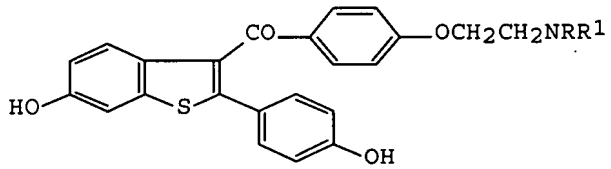

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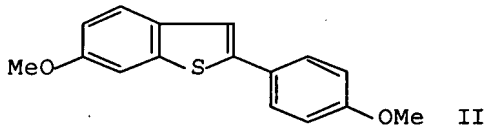

II

AB 3-[4-(2-Aminoethoxy)benzoyl]benzothiophenes I [R, R1 = C1-4 alkyl; RR1 = (CH2)4, (CH2)5, (CH2)6, CH2CHMeCH2CH2, CH2CH2OCH2CH2], useful as antiestrogens (no data), were prepared by acylating benzothiophene II. Thus, heating 3-MeOC6H4SCH2COC6H4OMe-4 with polyphosphoric acid gave II, which was acylated by 4-(Me2NCH2CH2O)C6H4CO2H.HCl and SOCl2 in PhCl-CH2Cl2 containing DMF and AlCl3 to give I (R = R1 = Me).

L6 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:71917 CAPLUS Full-text
DOCUMENT NUMBER: 98:71917
TITLE: Benzothiophene compounds
INVENTOR(S): Jones, Charles David
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 107 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62503	A1	19821013	EP 1982-301737	19820401
R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8282265	A	19821007	AU 1982-82265	19820401
AU 555658	B2	19861002		
GB 2097788	A	19821110	GB 1982-9680	19820401
GB 2097788	B	19850424		
JP 57181081	A	19821108	JP 1982-56479	19820402
PRIORITY APPLN. INFO.:			US 1981-246335 A	19810403
			US 1981-331045 A	19811216

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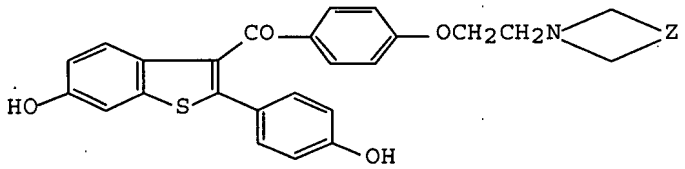

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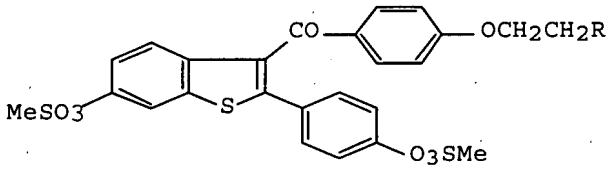

II

AB [(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were prepared, and limited the increase of uterine weight in rats treated with estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).

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